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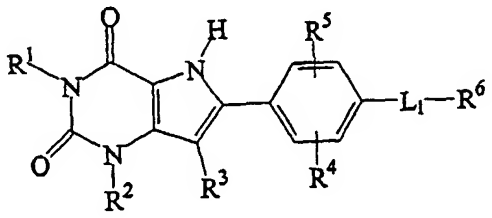
(54) Title: 6-PHENYLDIHYDROPYRROLOPYRIMIDINEDIONE DERIVATIVES



(I)

(57) Abstract: 6-phenylpyrrolopyrimidinedione derivatives of the formula (I), and pharmaceutically acceptable salts thereof, wherein R^1,R^2,R^3,R^4 and R^5 are organic residues, L_1 is a spacer group and R^6 is $C(O)NR^{10}R^{11}$, $-S(O)_2NR^{10}R^{11}$,?¿-ON=CR $^{12}R^{13}$, or a heterocyclyl, aryl?¿or heteroaryl group, where R^{10}, R^{11}, R^{12} and R^{13} are organic residues, have therapeutic potential as A2 adenosine receptor inhibitors.

6-PHENYLDIHYDROPYRROLOPYRIMIDINEDIONE DERIVATIVES

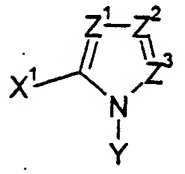
The present invention relates to antagonists of A2 adenosine receptors and in particular to antagonists of the A2b adenosine receptor subtype. Such antagonists are useful in preventing mast cell degranulation and are therefore useful in the treatment, prevention or suppression of disease states induced by activation of the A2b receptor and mast cell activation. These disease states include but are not limited to asthma, myocardial reperfusion injury, allergic reactions including but not limited to rhinitis, poison ivy induced responses, urticaria, scleroderm arthritis, other autoimmune diseases and inflammatory bowel diseases.

Adenosine regulates several physiological functions through specific cell membrane receptors. Four distinct adenosine receptors have been identified and classified as A1, A2a, A2b and A3, which are members of the G-protein coupled receptor family. The A2b adenosine receptor subtype (see review Feoktistov, I., Biaggioni, I. *Pharmacol. Rev.* 1997, *49*, 381-402) has been identified in a variety of human and murine tissues and appears to be involved in the control of vascular tone, regulation of vascular smooth muscle growth, regulation of the hepatic glucose production, modulation of intestinal tone as well as intestinal secretion and can also modulate mast cell degranulation mediating the response of human mast cells to adenosine. Adenosine A2a receptors modulate the release of GABA in the striatum, which possibly regulates the activity of medium spiny neurons. Thus, A2a receptor antagonists may be a useful treatment for Parkinson's disease not only as monotherapy but also in combination with L-DOPA and dopamine agonist drugs.

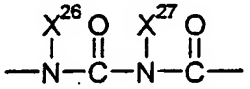
It has now, surprisingly, been found that certain 6-(substituted)phenyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione derivatives are potent and selective inhibitors of A2 adenosine receptors and in particular the A2b receptor subtype, and have efficacy in treating or preventing asthma, bronchoconstriction, allergic potentiation, inflammation or reperfusion injury, myocardial ischemia, inflammation, diarrheal diseases, brain arteriole diameter constriction, Parkinson's disease, insulin or

non insulin dependent diabetes mellitus, and/or release of allergic mediators.

EP 0 480 659 relates to compounds of general formula

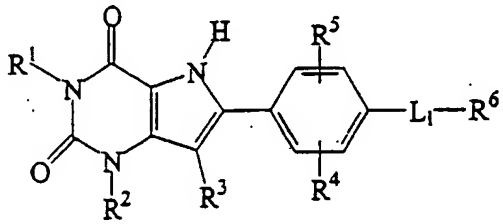


wherein each of Z^1, Z^2 and Z^3, independently represents: a nitrogen atom, a group represented by general formula: $=C(X^2)-$ or a group represented by general formula: $=C(X^3)-$. When Z^2 and Z^3 represent a group of general formula: $=C(X^2)-$ or a group of general formula: $=C(X^3)-$, X^2 and X^3 may be combined together to form a group represented by general formula:



and Y does not represent hydrogen; which possess angiotensin-II receptor antagonizing activity for the prevention or treatment of hyperuricemia.

The present invention provides a 6-phenylpyrrolopyrimidinedione derivative of the formula (I), or a pharmaceutically acceptable salt thereof,



(I)

wherein:

- R^1 and R^2 are the same or different and each represents hydrogen, a group of formula $-(CH_2)_n-R^7$, or an alkyl group which is unsubstituted or substituted by one or more, for example 1 or 2, substituents selected from hydroxy, alkoxy, alkylthio,

amino, mono- or di-alkylamino, hydroxycarbonyl, alkoxycarbonyl, acylamino, carbamoyl, alkylcarbamoyl, dihydroxyphosphoryloxy and dialkoxyphosphoryloxy groups,

wherein n is an integer of from 0 to 4 and R^7 represents a cycloalkyl group, a phenyl group or a cyclic group which is a 3- to 7-membered, aromatic or non-aromatic ring, which contains from 1 to 4 heteroatoms selected from N, O and S and which is optionally fused to an aromatic or heteroaromatic ring, the phenyl group being unsubstituted or substituted by one or more, for example 1, 2, 3 or 4, substituents selected from halogen, alkyl, aryl, heteroaryl, heterocyclyl, hydroxy, alkylenedioxy, alkoxy, alkylthio, amino, mono- or di-alkylamino, nitro, cyano, hydroxycarbonyl, alkoxycarbonyl, acylamino, carbamoyl, alkylcarbamoyl, dihydrophosphoryloxy, dialkoxyphosphoryloxy and haloalkyl groups and the cyclic group being unsubstituted or substituted by one or more, for example 1, 2, 3 or 4, substituents selected from halogen, hydroxy, alkoxy, phenyl, alkoxycarbonyl, amino, mono-alkylamino, di-alkylamino, hydroxycarbonyl, and alkyl groups, the alkyl substituents being unsubstituted or substituted by one or more, for example 1 or 2, further substituents selected from halogen, hydroxy, alkoxy, alkylthio, acylamino, carbamoyl, alkylcarbamoyl, dihydroxyphosphoryloxy, dialkoxyphosphoryloxy, hydroxyalkoxy, phenyl, alkoxycarbonyl, amino, mono- and di-alkylamino and hydroxycarbonyl groups;

- R^3 represents hydrogen, halogen, or a nitro, alkoxycarbonyl or alkyl group, the alkyl group being unsubstituted or substituted by one or more, for example 1 or 2, substituents selected from hydroxy, halogen, alkoxy, alkylthio, amino, mono- or di-alkylamino, hydroxycarbonyl, alkoxycarbonyl, acylamino, carbamoyl and alkylcarbamoyl groups;

- R^4 and R^5 are the same or different and each represents hydrogen, halogen, alkyl, hydroxy, alkoxy, alkylthio, dialkylaminoalkoxy, amino, mono- or dialkylamino, nitro, cyano or haloalkyl, or R^4 and R^5, together with the atoms to which they are attached, form a 5 to 7 membered ring containing from 0 to 4 heteroatoms selected from N, O and S;

- L_1 is a direct bond or is -O-, -S-, -N(Z)-, -S(CR^8R^9)$_m$-, -O(CH_2)$_m$-, -O(CR^8R^9)$_m$-, -CH=CH-, -(CH_2)$_m$-, -(CR^8R^9)$_m$-, -(CH_2)$_m$O-, -(CR^8R^9)$_m$O-, -(CR^8R^9)$_m$N(Z)-, -O(CH_2)$_m$O-, -O(CR^8R^9)$_m$O-, or -N(Z)(CR^8R^9)$_m$- wherein m is an integer of from 1 to 6, preferably an integer of from 1 to 4, and either Z, R^8 and R^9 are the same or different and each represent a group selected from hydrogen, C_1-C_6 alkyl, cycloalkyl, cycloalkyl-C_1-C_6 alkyl, heterocyclyl, heterocyclyl-C_1-C_6 alkyl, aryl, aryl-C_1-C_6 alkyl, heteroaryl, heteroaryl-C_1-C_6 alkyl, hydroxy, C_1-C_6 alkoxy, halogen, cyano, C_1-C_6 alkoxycarbonyl, carbamoyl and haloalkyl, the alkyl, cycloalkyl, heterocyclyl, aryl and heteroaryl moieties being unsubstituted or substituted with one to four substituents independently selected from R^1, or Z is as defined above and R^8 and R^9, together with the atom to which they are attached, form a 4 to 8 membered ring; and

- R^6 represents -C(O)$NR^{10}R^{11}$, -S(O)$_2$$NR^{10}R^{11}$, -ON=$CR^{12}R^{13}$, or a heterocyclyl, aryl or heteroaryl group, the heterocyclyl, aryl and heteroaryl groups being unsubstituted or substituted with substituents R^{14} to R^{17}, wherein:

R^{10} and R^{11} are either

(a) the same or different, each independently representing hydrogen, an alkyl group, a cycloalkyl group or a phenyl group, wherein (i) the alkyl group is unsubstituted or substituted by one or more, for example 1 or 2, substituents selected from hydroxy, halogen, alkoxy, alkylthio, amino and mono- and di-alkylamino groups, (ii) the cycloalkyl group is optionally fused to an aromatic ring and (iii) the cycloalkyl group and the phenyl group are unsubstituted or substituted by one or more, for example 1, 2, 3 or 4, substituents selected from (1) groups of formula -(CH_2)$_n$ R^7, -O-(CH_2)$_n$ R^7, -S-(CH_2)$_n$ R^7, -COR and -CONHR, wherein R is alkyl or -(CH_2)$_n$$R^7$ and n and R^7 are as defined above, (2) groups of formula -(CH_2)$_n$-S(O)$_2$$NR'R''$ wherein n is as defined above and R' and R'' are the same or different and are each selected from hydrogen and alkyl or form, together with the nitrogen atom to which they are attached, a 4- to 7- membered heterocyclic ring containing 1, 2 or 3 heteroatoms selected from N, O, and S, (3) groups of formula -(CH_2)$_n$-CO_2R''' wherein n is as defined above and R''' is hydrogen or alkyl, (4) groups of formula -N^+ R''''_3, wherein each R'''' is the same or different and is an alkyl

group, and (5) halogen atoms and alkyl, hydroxy, alkylenedioxy, alkoxy, alkylthio, amino, mono- and di-alkylamino, nitro, cyano, hydroxycarbonyl, alkoxycarbonyl, acylamino, carbamoyl, dihydroxyphosphoryloxy, dialkoxyphosphoryloxy or haloalkyl groups, the alkyl substituents being unsubstituted or substituted by one or more, for example 1 or 2, further substituents selected from cyano, nitro, amino, hydroxy and halogen,

(b) together with the atom to which they are attached, a 3- to 7-membered ring comprising up to 4 heteroatoms selected from N, O and S, which ring is (i) optionally fused to an aromatic ring or to a heteroaromatic ring which is in turn optionally fused to an aromatic ring and is (ii) unsubstituted or substituted by one or more, for example 1, 2, 3 or 4, substituents independently selected from halogen atoms, groups of formula -X-R^7 and -CO_2-X-R^7 wherein X is a direct bond, a C_1-C_4 alkylene group or a carbonyl group, for example a direct bond or a C_1-C_4 alkylene group, and R^7 is as defined above, and hydroxy, cyano, nitro, oxoalkyl, carbamoyl, hydroxycarbonyl, alkoxycarbonyl, amino, mono- and di-alkylamino, divalent alkylene and alkyl groups, the alkyl substituents being unsubstituted or substituted by one or more, for example 1 or 2, further substituents selected from hydroxy, alkoxy, hydroxyalkoxy, amino and mono- and di-alkylamino groups, and the moiety X being unsubstituted or substituted by one or two further substituents selected from phenyl, alkyl, hydroxy and thio groups and groups of formula -CO_2R' and -CONR'R" wherein R' and R" are the same or different and are hydrogen or alkyl or

(c) defined so that R^{10} represents hydrogen or an alkyl group and R^{11} represents a group of formula -X-R^7 wherein X and R^7 are as defined above;

R^{12} and R^{13} are defined as R^{10} and R^{11} above, except that either or both of R^{12} and R^{13} can be an amino, alkylamino or dialkylamino group; and

R^{14} to R^{17} are the same or different and each independently represents hydrogen, a halogen atom, a group of formula -$(CH_2)_n$-R^7, wherein n and R^7 are as defined above or an alkyl group, for example hydrogen, a group of formula -$(CH_2)_n$-R^7 or an alkyl group, the alkyl group being unsubstituted or substituted by one or more, for example 1

or 2, substituents selected from hydroxy, alkoxy, alkylthio, amino, mono- or di-alkylamino, hydroxycarbonyl, alkoxycarbonyl, acylamino, carbamoyl, alkylcarbamoyl, dihydroxyphosphoryloxy, dialkoxyphosphoryloxy and haloalkyl groups, or R^{14} and R^{15} are as defined above and R^{16} and R^{17}, together with the atoms to which they are attached, form a 4 to 8 membered aromatic or non-aromatic ring which contains from 0 to 4 heteroatoms selected from N, O and S, and which is unsubstituted or substituted by one or more, for example 1, 2, 3 or 4, substituents selected from halogen atoms and alkyl, hydroxy, phenyl, alkoxycarbonyl, amino, mono-alkylamino, di-alkylamino and hydroxycarbonyl groups, the alkyl substituents being unsubstituted or substituted by one or more, for example 1 or 2, further substituents selected from halogen atoms and hydroxy, alkoxy, alkylthio, acylamino, carbamoyl, alkylcarbamoyl, dihydroxyphosphoryloxy, dialkoxyphosphoryloxy, hydroxyalkoxy, phenyl, alkoxycarbonyl, amino, mono- or di-alkylamino and hydroxycarbonyl groups.

As used herein, an alkyl group or moiety is typically a linear or branched alkyl group or moiety containing from 1 to 6 carbon atoms, such as a C_1-C_4 alkyl group or moiety, for example methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl and t-butyl. Where a group contains two or more alkyl moities, the alkyl moieties may be the same or different. When an alkyl group or moiety carries 2 or more substituents, the substituents may be the same or different.

As used herein, an alkylenedioxy group or moiety is a linear or branched group or moiety containing from 1 to 6, for example from 1 to 4, carbon atoms. Examples include methylenedioxy, ethylenedioxy, propylenedioxy and butylenedioxy. When an alkylenedioxy group or moiety carries 2 or more substituents, the substituents may be the same or different.

As used herein, an alkylene group is a divalent alkyl moiety typically having from 1 to 6, for example from 1 to 4, carbon atoms. Examples of C_1-C_4 alkylene groups include methylene, ethylene, propylene and butylene groups.

As used herein, an aryl group or moiety is typically a C_6-C_{10} aryl group or moiety such as phenyl or naphthyl. Phenyl is preferred. When an aryl group or moiety carries 2 or more substituents, the substituents may be the same or different.

As used herein, a heteroaryl group or moiety is typically a 5- to 10- membered aromatic ring, such as a 5- or 6- membered ring, containing at least one heteroatom selected from O, S and N. Examples include pyridyl, pyrazinyl, pyrimidinyl, pyridazinyl, furanyl, oxadiazolyl, oxazolyl, imidazolyl, thiazolyl, thiadiazolyl, thienyl, pyrazolidinyl, pyrrolyl and pyrazolyl groups. Oxadiazolyl, oxazolyl, pyridyl, pyrrolyl, imidazolyl, thiazolyl, thiadiazolyl, furanyl, pyrazinyl and pyrimidinyl groups are preferred. When a heteroaryl group or moiety carries 2 or more substituents, the substituents may be the same or different.

As used herein, a halogen is a typically chlorine, fluorine, bromine or iodine and is preferably chlorine, fluorine or bromine.

As used herein, a said alkoxy group or moiety is typically a said alkyl group attached to an oxygen atom. An alkylthio group or moiety is typically a said alkyl group attached to a thio group. A haloalkyl or haloalkoxy group is typically a said alkyl or alkoxy group substituted by one or more said halogen atoms. Typically, it is substituted by 1, 2 or 3 said halogen atoms. Preferred haloalkyl and haloalkoxy groups include perhaloalkyl and perhaloalkoxy groups such as $-CX_3$ and $-OCX_3$ wherein X is a said halogen atom. Particularly preferred haloalkyl groups are CF_3 and CCl_3. Particularly preferred haloalkoxy groups are $-OCF_3$ and $-OCCl_3$.

As used herein, a cycloalkyl group typically has from 3 to 6 carbon atoms. Examples include cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl. It is preferably cyclopropyl, cyclopentyl or cyclohexyl. When a cycloalkyl group carries 2 or more substituents, the substituents may be the same or different.

As used herein, a heterocyclyl group is typically a non-aromatic, saturated or unsaturated C_5-C_{10} carbocyclic ring in which one or more, for example 1, 2 or 3, of the carbon atoms are replaced by a heteroatom selected from N, O and S. Saturated heterocyclyl groups are preferred. Examples of suitable heterocyclyl groups include

piperidinyl, piperazinyl, morpholinyl, 4,5-dihydro-oxazolyl, 3-aza-tetrahydrofuranyl, imidazolidinyl and pyrrolidinyl groups. Where a heterocyclyl group carries 2 or more substituents, the substituents may be the same or different.

As used herein, an acyl group or moiety typically has from 2 to 7 carbon atoms. Thus, it is typically a group of formula -COR wherein R is a hydrocarbyl group having from 1 to 6 carbon atoms. Preferably, it is a group of formula -COR wherein R is a said C_1-C_6 alkyl group.

Compounds of the formula (I) containing one or more chiral centre may be used in enantiomerically or diastereoisomerically pure form, or in the form of a mixture of isomers.

As used herein, a pharmaceutically acceptable salt is a salt with a pharmaceutically acceptable acid or base. Pharmaceutically acceptable acids include both inorganic acids, for example hydrochloric, sulphuric, phosphoric, diphosphoric, hydrobromic and nitric acid and organic acids, for example citric, fumaric, maleic, malic, ascorbic, succinic, tartaric, benzoic, acetic, methanesulphonic, ethanesulphonic, benzenesulphonic or p-toluenesulphonic acid. Pharmaceutically acceptable bases include alkali metal (e.g. sodium or potassium) and alkali earth metal (e.g. calcium or magnesium) hydroxides and organic bases, for example alkyl amines, aralkyl amines and heterocyclic amines.

Typically, at least one of R^1 and R^2 is hydrogen or a said alkyl group.

Preferably, R^1 and R^2 are the same or different and each independently represent hydrogen, a group of formula $-(CH_2)_n-R^7$ wherein n and R^7 are as defined above or a C_1-C_6 alkyl group which is unsubstituted or substituted by one or more, for example 1 or 2, substituents selected from hydroxy, C_1-C_6 alkoxy, C_1-C_6 alkylthio, amino and mono- and di-(C_1-C_6 alkyl)amino groups.

When R^1 or R^2 is a group of formula $-(CH_2)_n-R^7$, R^7 is preferably a C_3-C_6 cycloalkyl group or a cyclic group which is a 5- or 6-membered non-aromatic ring containing 1 or 2 heteroatoms selected from N, O and S, for example a morpholino group. In this embodiment, R^7 is, for example, a C_3-C_6 cycloalkyl group.

More preferably, R^1 and R^2 are the same or different and each independently represent hydrogen, a C_1-C_4 alkyl group which is unsubsituted or substituted by 1 or 2 substituents selected from C_1-C_4 alkoxy and C_1-C_4 alkylthio substituents, a group of formula -$(CH_2)_n$-(C_3-C_6 cycloalkyl) or -$(CH_2)_n$-(morpholino) wherein n is as defined above. Examples of the more preferable R^1 and R^2 groups are hydrogen, a C_1-C_4 alkyl group which is unsubsituted or substituted by 1 or 2 substituents selected from C_1-C_4 alkoxy and C_1-C_4 alkylthio substituents or a group of formula -$(CH_2)_n$-(C_3-C_6 cycloalkyl) wherein n is as defined above.

More preferably still, R^1 and R^2 are the same or different and each independently represents a C_1-C_4 alkyl group, for example methyl, ethyl and n-propyl.

Preferably, R^3 represents hydrogen, halogen or a C_1-C_6 alkyl group which is unsubstituted or substituted by one or more, for example 1 or 2, substituents selected from halogen atoms and hydroxy groups.

More preferably, R^3 represents hydrogen, halogen, for example chlorine and bromine, or C_1-C_4 haloalkyl, for example -CF_3 or -CCl_3. More preferably still, R^3 represents hydrogen or halogen, for example chlorine and bromine.

Typically, when R^4 and/or R^5 represents a haloalkyl group, the haloalkyl group is a trifluoromethyl group.

Preferably, R^4 and R^5 are the same or different and each represents hydrogen, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, hydroxy, C_1-C_6 alkoxy, C_1-C_6 alkylthio, amino or mono- or di-(C_1-C_6 alkyl)amino.

More preferably, R^4 and R^5 are the same or different and each represents hydrogen, C_1-C_6 alkyl, hydroxy, C_1-C_6 alkoxy, C_1-C_6 alkylthio, amino or C_1-C_6 alkylamino.

More preferably still, R^4 and R^5 are the same or different and represent hydrogen, C_1-C_4 alkyl, C_1-C_4 alkoxy, for example methoxy, or C_1-C_4 alkylthio, for example methylthio.

Typically, when Z, R^8 and/or R^9 contains a cycloalkyl, heterocyclyl, aryl or heteroaryl moiety, the cycloalkyl, heterocyclyl, aryl or heteroaryl moiety is

unsubstituted or substituted by 1 or 2 C_1-C_4 alkyl groups. Typically, when R^8 and/or R^9 contains an alkyl moiety, the alkyl moiety is unsubstituted.

When Z, R^8 and/or R^9 is haloalkyl, the haloalkyl group is typically $-CFH_2$, $-CF_2H$ or $-CF_3$.

Typically, Z, R^8 and R^9 are the same or different and each represents hydrogen, C_1-C_4 alkyl, C_3-C_6 cycloalkyl, (C_3-C_6 cycloalkyl)-(C_1-C_4 alkyl)-, phenyl or phenyl-(C_1-C_4 alkyl)-. Preferably, Z, R^8 and R^9 are the same or different and each represents hydrogen, C_1-C_6 alkyl, for example methyl and ethyl, or phenyl. For example, Z, R^8 and R^9 are the same or different and each represents C_1-C_6 alkyl, for example methyl and ethyl, or phenyl.

Preferably, L_1 is a direct bond or $-O(CH_2)_m-$, $-O(CR^8R^9)_m-$, $-S(CR^8R^9)_m-$, $-CH=CH-$, $-(CH_2)_m-$, $-(CR^8R^9)_m-$, $-(CH_2)_mO-$, $-(CR^8R^9)_mO-$, $-O(CH_2)_mO-$, $-(CR^8R^9)_mN(Z)-$ or $-N(Z)(CR^8R^9)_m-$, for example, a direct bond or $-O(CH_2)_m-$, $-O(CR^8R^9)_m-$, $-S(CR^8R^9)_m-$, $-CH=CH-$, $-(CH_2)_m-$, $-(CR^8R^9)_m-$, $-(CH_2)_mO-$, $-(CR^8R^9)_mO-$, $-(CR^8R^9)_mN(Z)-$ or $-N(Z)(CR^8R^9)_m-$, wherein m is from 1 to 4, and is preferably 1, 2 or 3, R^8 and R^9 are as defined above and Z is hydrogen or C_1-C_4 alkyl.

More preferably, L_1 is $-O(CH_2)_m-$, $-O(CR^8R^9)_m-$, $-CH=CH-$, $-(CH_2)_m-$, $-(CR^8R^9)_m-$, $-(CH_2)_mO-$, $-C(R^8R^9)_mO-$, $-O(CH_2)_mO-$ or $-(CR^8R^9)_mN(Z)-$, for example, $-O(CH_2)_m-$, $-O(CR^8R^9)_m-$, $-CH=CH-$, $-(CH_2)_m-$, $-(CR^8R^9)_m-$, $-(CH_2)_mO-$ or $-(CR^8R^9)_mO-$, such as $-O(CH_2)_m-$, $-O(CR^8R^9)_m-$, $-CH=CH-$, $-(CH_2)_m-$, $-(CR^8R^9)_m-$ or $-(CH_2)_mO-$, wherein m is from 1 to 4, and is preferably 1, 2 or 3, and R^8 and R^9 are as defined above and are preferably hydrogen, C_1-C_6 alkyl, for example methyl and ethyl, or phenyl.

More preferably, L_1 is $-O-CH_2-$, $-CH_2O-$ or $-CH_2NH-$, for example $-O-CH_2$.

The groups L_1 are herein written such that the left hand end of the group is attached to the phenyl moiety in formula (I) and the right hand end is attached to R^6. Thus, for example, when L_1 represents $-CH_2NH-$, the $-CH_2-$ moiety is attached to the phenyl ring whilst the $-NH-$ moiety is attached to R^6.

R^{12} and R^{13} in the group R^6 are either

(a) the same or different, each independently representing amino, alkylamino, dialkylamino, hydrogen, an alkyl group a cycloalkyl group or a phenyl group, wherein (i) the alkyl group is unsubstituted or substituted by one or more, for example 1 or 2, substituents selected from hydroxy, halogen, alkoxy, alkylthio, amino or mono- or di-alkylamino groups, (ii) the cycloalkyl group is optionally fused to an aromatic ring and (iii) the cycloalkyl group and the phenyl group are unsubstituted or substituted by one or more, for example 1, 2, 3 or 4, substituents selected from (1) groups of formula $-(CH_2)_nR^7$, $-O-(CH_2)_nR^7$, $-S-(CH_2)_nR^7$, -COR and –CONHR, wherein R is alkyl or $-(CH_2)_nR^7$ and n and R^7 are as defined above, (2) groups of formula $-(CH_2)_n-S(O)_2NR'R''$ wherein n is as defined above and R' and R'' are the same or different and are each selected from hydrogen and alkyl or form, together with the nitrogen atom to which they are attached, a 4- to 7- membered heterocyclic ring containing 1, 2 or 3 heteroatoms selected from N, O, and S, (3) groups of formula $-(CH_2)_n-CO_2R'''$, wherein n is as defined above and R''' is hydrogen or alkyl, (4) groups of formula $-N^+R''''_3$ wherein each R'''' is the same or different and is an alkyl group, and (5) halogen atoms and alkyl, hydroxy, alkylenedioxy, alkoxy, alkylthio, amino, mono- or di-alkylamino, nitro, cyano, hydroxycarbonyl, alkoxycarbonyl, acylamino, carbamoyl, dihydroxyphosphoryloxy, dialkoxyphosphoryloxy or haloalkyl groups, the alkyl substituents being unsubstituted or substituted by one or more, for example 1 or 2, further substituents selected from cyano, nitro, amino, hydroxy and halogen,

(b) together with the atom to which they are attached, a 3 to 7-membered ring comprising up to 4 heteroatoms selected from N, O and S, which ring is optionally fused to one or two rings selected from aromatic and heterocyclyl rings and is unsubstituted or substituted by one or more, for example 1, 2, 3 or 4, substituents independently selected from halogen atoms, groups of formula $-X-R^7$ and $-CO_2-X-R^7$ wherein X is a direct bond or a C_1-C_4 alkylene group and R^7 is as defined above, and hydroxy, cyano, nitro, oxoalkyl, carbamoyl, hydroxycarbonyl, alkoxycarbonyl, amino, mono- and di-alkylamino, divalent alkylene and alkyl groups, the alkyl substituents being unsubstituted or substituted by one or more, for example 1 or 2, further

substituents selected from hydroxy, alkoxy, hydroxyalkoxy, amino or mono- or di-alkylamino groups, and the moiety X being unsubstituted or substituted by one or two further substituents selected from phenyl, alkyl, hydroxy and thio groups and groups of formula $-CO_2R'$ and $-CONR'R''$ wherein R' and R" are the same or different and are hydrogen or alkyl, or

(c) defined so that R^{12} represents hydrogen or an alkyl group and R^{13} represents a group of formula $-X-R^7$ wherein X and R^7 are as defined above.

Preferably, R^{12} and R^{13} are the same or different and each represents hydrogen, amino, (C_1-C_6 alkyl)amino, di-(C_1-C_6 alkyl)amino, C_1-C_6 alkyl, C_3-C_6 cycloalkyl or phenyl, the alkyl moieties being unsubsituted or substituted by 1 or 2 subsitutents selected from hydroxy groups and halogen atoms and the cycloalkyl group and the phenyl group being unsubstituted or substituted by 1, 2, 3 or 4 substituents selected from halogen atoms and C_1-C_4 alkoxy, C_1-C_4 alkylthio, C_1-C_4 alkyl, hydroxy, C_1-C_4 haloalkyl, amino, and mono-and di-(C_1-C_4 alkyl)amino groups.

More preferably, R^{12} and R^{13} are the same or different and each represents amino, mono- or di-(C_1-C_4 alkyl)amino, or phenyl, the phenyl group being unsubstituted or substituted by one or two substituents selected from halogen, for example fluorine, C_1-C_4 alkoxy, for example methoxy, C_1-C_4 alkyl, for example methyl and ethyl, hydroxy, amino, mono-(C_1-C_4 alkyl)-amino and C_1-C_4 haloalkyl, for example $-CF_3$ and $-CCl_3$.

Most preferably, R^{12} is amino and R^{13} is a phenyl group which is unsubstituted or substituted with a halogen atom, for example a fluorine atom.

When the moiety R^7 is a phenyl group which carries one or more haloalkyl substituent, the or each haloalkyl substituent is typically $-CF_3$.

When the moiety R^7 is a said 3- to 7- membered ring which is fused to an aromatic or heteroaromatic ring, the 3- to 7- membered ring is typically fused to an aromatic ring. Preferably, it is fused to a phenyl group. Preferably, such fused ring moieties are 5- membered heteroaromatic rings containing 1 or 2 heteroatoms selected

from N, O and S, fused to a phenyl group. Examples include benzimidazole and benzothiazole.

Preferably, R^7 is:

- a C_3-C_6 cycloalkyl group;
- a phenyl group which is unsubstituted or substituted with 1, 2 or 3 substituents selected from halogen, C_1-C_4 alkyl, aryl, for example phenyl, heteroaryl, hydroxy, C_1-C_4 alkylenedioxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, amino, mono- and di-(C_1-C_4 alkyl)amino, nitro, cyano, hydroxycarbonyl, (C_1-C_4 alkoxy)carbonyl, (C_2-C_7 acyl)amino, carbamoyl, (C_1-C_4 alkyl)carbamoyl, dihydrophosphoryloxy, di-(C_1-C_4 alkoxy)phosphoryloxy and C_1-C_4 haloalkyl groups; or
- a cyclic group which is a 3- to 7- membered aromatic or non-aromatic ring containing from 1 to 4, for example 1, 2 or 3, heteroatoms selected from N, O and S which is optionally fused to an aromatic ring, which group is unsubstituted or substituted by 1, 2 or 3 substituents selected from halogen, hydroxy, C_1-C_4 alkoxy, phenyl, C_1-C_4 alkoxycarbonyl, amino, mono-(C_1-C_4 alkyl)amino, di-(C_1-C_4 alkyl)amino, hydroxycarbonyl and C_1-C_4 alkyl groups, the alkyl substituents being unsubstituted or substituted by 1 or 2 further substituents selected from halogen, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, C_2-C_7 acylamino, carbamoyl, C_1-C_4 alkylcarbamoyl, dihydroxyphosphoryloxy, di-(C_1-C_4 alkoxy)phosphoryloxy, hydroxy-(C_1-C_4 alkoxy)-, phenyl, C_1-C_4 alkoxycarbonyl, amino, mono- and di-(C_1-C_4 alkyl)amino and hydroxycarbonyl groups.

Preferably, the cyclic group is a 5- or 6- membered aromatic or non-aromatic ring containing 1 or 2 heteroatoms selected from N, O and S, which is optionally fused to a phenyl ring. More preferably, the cyclic group is a pyridinyl, pyrazinyl, pyrimidinyl, imidazolyl, thiazolyl, oxazolyl, isoxazolyl, pyrazolyl, piperidinyl, thiadiazolyl, furanyl, benzimidazolyl, benzothiazolyl, morpholino or thienyl group. For example, the cyclic group is a pyridinyl, pyrazinyl, pyrimidinyl, imidazolyl, thiazolyl, oxazolyl, piperidinyl, thiadiazolyl, furanyl, benzimidazolyl or benzothiazolyl group. Further, the substituents on the cyclic group are preferably selected from halogen, for

example chlorine, hydroxy, phenyl, C_1-C_4 alkoxy, amino, mono- and di-(C_1-C_4 alkyl)amino, C_1-C_4 alkyl, C_1-C_4 haloalkyl, for example $-CF_3$, hydroxy-(C_1-C_4 alkyl)- and phenyl-(C_1-C_4 alkyl)-, for example benzyl. More preferably, these subsitutents are selected from hydroxy, chlorine, C_1-C_4 alkyl, $-CF_3$, phenyl and benzyl.

Preferably, when R^7 is a phenyl group, it is a phenyl group which is unsubstituted or substituted by 1 or 2 subsitutents selected from halogen, for example fluorine and chlorine, C_1-C_4 alkyl, phenyl, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, amino, mono- and di-(C_1-C_4 alkyl)amino and C_1-C_4 haloalkyl groups. More preferably, these substituents are selected from halogen, for example fluorine and chlorine, C_1-C_4 alkyl, for example methyl and ethyl, C_1-C_4 alkoxy, for example methoxy and ethoxy, hydroxy, C_1-C_4 alkylthio and $-CF_3$.

Typically, when the moiety X is substituted, R^7 is a said phenyl group. More typically, when X is substituted, R^7 is an unsubstituted phenyl group. Preferred substitutents on the moiety X include phenyl, C_1-C_4 alkyl, hydroxy, $-CO_2H$ and $-CO_2$-(C_1-C_4 alkyl). More preferably, the substituents on the X moiety are selected from hydroxy, $-CO_2Me$, $-CO_2H$, methyl and phenyl.

When R^{10} and R^{11} are defined according to option (a) above, R^{10} and/or R^{11} can be a cycloalkyl group which is optionally fused to an aromatic ring. When the cycloalkyl group is fused to an aromatic ring, it is typically fused to a phenyl ring. Examples of such fused rings include a cyclohexyl ring fused to a phenyl ring and a cyclopentyl ring fused to a phenyl ring.

Typically, when R^{10} and R^{11} are defined according to option (a) above, at least one of R^{10} and R^{11} is hydrogen or C_1-C_6 alkyl.

When R^{10} and R^{11} are defined according to option (a) above, preferably they are the same or different and each independently represent hydrogen, a C_1-C_6 alkyl group, a C_5-C_6 cycloalkyl group optionally fused to a phenyl ring or a phenyl group, the alkyl group being unsubstituted or substituted by 1 or 2 substituents selected from hydroxy, halogen, C_1-C_4 alkoxy and amino groups and the phenyl and cycloalkyl groups being unsusbtituted or substituted by 1, 2, 3 or 4 substituents selected from (1) groups of

formula $-(CH_2)_n R^7$, $-O-(CH_2)_n-R^7$, $-S-(CH_2)_n-R^7$ and -COR and -CONHR wherein R is C_1-C_6 alkyl or $-(CH_2)_n R^7$ and n and R^7 are as defined above, (2) groups of formula $-(CH_2)_n-S(O)_2NR'R''$ wherein n is as defined above and R' and R'' are the same or different and are each selected from hydrogen and C_1-C_6 alkyl or form, together with the N atom to which they are attached, a 4- or 5-membered saturated heterocyclic ring containing 1 or 2 heteroatoms selected from N, O and S, (3) groups of formula $-(CH_2)_n-CO_2R'''$ wherein n is as defined above and R''' is hydrogen or C_1-C_6 alkyl, (4) groups of formula $-NR''''_3$, wherein each R'''' is the same or different and is a C_1-C_6 alkyl group, and (5) halogen atoms and C_1-C_6 alkyl, hydroxy, C_1-C_4 alkylenedioxy, C_1-C_6 alkoxy, C_1-C_6 alkythio, amino, mono- and di-(C_1-C_6 alkyl)amino, nitro, cyano, hydroxycarbonyl, (C_1-C_6 alkoxy)carbonyl, (C_2-C_7 acyl)amino, carbamoyl, and C_1-C_6 haloalkyl groups, the alkyl substituents being unsubstituted or substituted by one or more, for example 1 or 2, further substituents selected from cyano, nitro, amino, hydroxy and halogen.

More preferably, when R^{10} and R^{11} are defined according to option (a) above, they are the same or different and each represent hydrogen, a C_1-C_6 alkyl group, for example methyl and ethyl, a phenyl group or a C_5-C_6 cycloalkyl group optionally fused to a phenyl ring, the alkyl group being unsubstituted or substituted by 1 or 2 substituents selected from hydroxy, halogen and amino groups and the phenyl and cycloalkyl groups being unsubstituted or substituted by 1, 2 or 3 substituents selected from (1) groups of formula $-(CH_2)_n R^7$, $-O-(CH_2)_n-R^7$, -COR and -CONHR wherein R is C_1-C_4 alkyl or $-(CH_2)_n R^7$, n is 0, 1 or 2 and R^7 is as defined above, (2) groups of formula $-(CH_2)_n-S(O)_2-NR'R''$ wherein n is 0 or 1 and R' and R'' are the same or different and are hydrogen or C_1-C_4 alkyl or, together with the N atom to which they are attached, form a pyrrolidinyl or piperidyl ring, (3) groups of formula $-(CH_2)_n-CO_2R'''$, wherein n is 1 or 2 and R''' is hydrogen or C_1-C_4 alkyl, (4) groups of formula $-NR''''_3$ wherein each R'''' is the same or different and is a C_1-C_4 alkyl group, and (5) halogen atoms and C_1-C_4 alkyl, hydroxy, C_1-C_4 alkoxy, amino, mono- and di(C_1-C_4 alkyl)amino, nitro, cyano, hydroxycarbonyl, C_1-C_4 alkoxycarbonyl, (C_3-C_5 acyl)amino, carbamoyl and C_1-C_4

haloalkyl groups, the alkyl substituents being unsubstituted or substituted by a further substituent selected from cyano, nitro, amino, hydroxy and halogen.

Typically, when R^{10} and R^{11} are as defined in the preceding paragraph, R^7 is a phenyl group or a 5- or 6- membered aromatic or non-aromatic heterocycle having 1 or 2 heteroatoms selected from N, O and S, for example 4,5-dihydroxazolyl, the heterocycle being unsubstituted or substituted by 1 or 2 substituents selected from C_1-C_4 alkyl groups and the phenyl group being unsubstituted or substituted by 1 or 2 substituents selected from halogen atoms and C_1-C_4 alkyl and C_1-C_4 alkoxy groups.

Most preferably, when R^{10} and R^{11} are defined according to option (a) above, R^{10} is hydrogen and R^{11} is a phenyl group which is unsubstituted or substituted by one or two substituents selected from halogen atoms, for example fluorine and bromine, and phenyl and benzyloxy groups.

When R^{10} and R^{11} are defined according to option (b) above, R^{10} and R^{11} form a 3- to 7- membered heterocycle which is optionally fused to an aromatic ring or to a heteroaromatic ring which is in turn optionally fused to an aromatic ring. When the 3- to 7- membered heterocycle is fused to another ring, it is typically fused to a phenyl ring and/or to a 5- or 6- membered heterocyclic ring which is in turn optionally fused to a phenyl ring. Preferably, when the 3- to 7- membered ring is fused to another ring it is fused to a phenyl ring or to an indole group. Examples of such fused rings include 1,2,3,4-tetrahydroquinoline, 1,2,3,4-tetrahydroisoquinoline, 5;6,7,8-tetrahydro-8-aza-carbazole and 1,3,4,9-tetrahydro-beta-carbolinyl rings, for example 1,2,3,4-tetrahydroquinoline, 1,2,3,4-tetrahydroisoquinoline and 5,6,7,8-tetrahydro-8-aza-carbazole rings.

When R^{10} and R^{11} are defined according to option (b) above, they typically form, together with the N atom to which they are attached, a 3- to 7- membered ring containing from 1 to 4 heteroatoms selected from N, O and S, which ring is (i) optionally fused to an aromatic ring or to a heteroaromatic ring which is in turn optionally fused to an aromatic ring and is (ii) substituted or unsubstituted by 1, 2 or 3 substituents independently selected from halogen atoms, groups of formula -X-R^7 and

$-CO_2-X-R^7$ wherein X and R^7 are as defined above, and hydroxy, cyano, nitro, carbamoyl, hydroxycarbonyl, C_1-C_6 alkoxycarbonyl, amino, mono- and di-(C_1-C_6 alkyl)amino, divalent alkylene and C_1-C_6 alkyl groups, the alkyl substituents being unsubtituted or substituted by 1 or 2 further substituents selected from hydroxy and amino groups.

More preferably, when R^{10} and R^{11} are defined according to option (b) above, they form, together with the nitrogen atom to which they are attached, an aromatic or non-aromatic, for example non-aromatic, 5- or 6- membered ring containing 1 or 2 heteroatoms selected from N, O and S, which ring is optionally fused to a phenyl ring or to an indole group, and is unsubstituted or substituted by 1, 2 or 3 substituents independently selected from halogen atoms, groups of formula $-X-R^7$ and $-CO_2-X-R^7$ wherein X and R^7 are as defined above, and hydroxy, cyano, nitro, C_1-C_4 alkoxycarbonyl, amino, C_1-C_2 divalent alkylene, for example methylene and C_1-C_4 alkyl groups. The aromatic or non-aromatic ring is, for example, unsubstituted or substituted by 1, 2 or 3 substituents independently selected from halogen atoms, groups of formula $-X-R^7$ and $-CO_2-X-R^7$ wherein X and R^7 are as defined above, and hydroxy, cyano, nitro, amino, C_1-C_2 divalent alkylene, for example methylene and C_1-C_4 alkyl groups.

Typically, when R^{10} and R^{11} are as defined in the preceding paragraph, the said aromatic or non-aromatic 5- or 6- membered ring is a piperidinyl, piperazinyl, pyrazolyl or morpholino ring, for example a piperidinyl, piperazinyl or morpholino ring. It can be fused to a phenyl ring to form, for example, a tetrahydroquinoline or tetrahydroisoquinoline group, or to an indole group to form, for example a 5,6,7,8-tetrahydro-8-aza-carbazole ring or a 1,3,4,9-tetrahydro-beta-carbolinyl ring. Further, when R^{10} and R^{11} are as defined in the preceding paragraph, typically, X is a direct bond, a C_1-C_4 alkylene group or a carbonyl group, for example a direct bond or a C_1-C_4 alkylene group, wherein the C_1-C_4 alkylene group is unsubstituted or substituted by a phenyl group, and R^7 is a phenyl group or a cyclic group which is a 5- or 6- membered heteroaryl group containing 1 or 2 heteroatoms selected from N, O and S, which is optionally fused to a phenyl ring, the phenyl group and the cyclic group being

unsubstituted or substituted by 1 or 2 substituents selected from halogen atoms and C_1-C_4 alkyl, C_1-C_4 alkoxy and C_1-C_4 haloalkyl groups. Preferably, when R^{10} and R^{11} are as defined in the preceding paragraph, X is a direct bond, -CH_2-, -CH-Ph- or a carbonyl group, for example a direct bond, -CH_2- or -CH-Ph-, and R_7 is a pyridinyl, pyrimidyl, pyrazinyl, benzimidazoyl, benzothiazolyl or phenyl group, which group is unsubstituted or substituted by 1 or 2 substitutents selected from halogen atoms, and C_1-C_4 alkyl, C_1-C_4 alkoxy and -CF_3 groups.

Most preferably, when R^{10} and R^{11} are defined according to option (b) above they form, together with the N atom to which they are attached, a 1,2,3,4-tetrahydroisoquinoline group, a 1,3,4,9-tetrahydro-beta-carbolinyl group, a piperidine group or a piperazine group, for example, a 1,2,3,4-tetrahydroisoquinoline group, a piperidine group or a piperazine group, the piperidine and piperazine-groups being unsubstituted or subtituted by 1 or 2 substituents selected from phenyl, pyridinyl and hydroxy groups, the phenyl and pyridinyl groups being optionally further substituted by one or two halogen atoms, for example chlorine atoms. The piperidine and piperazine groups are, for example, substituted by one or two phenyl groups.

When R^{10} and R^{11} are defined according to option (c) above, typically, R^{10} represents hydrogen or a C_1 to C_6 alkyl group and R^{11} represents a group of formula -X-R^7, wherein X and R^7 are as defined above.

Typically, when R_{10} and R_{11} are defined according to option (c) above, R^{10} is hydrogen or a C_1-C_4 alkyl group and R^{11} is a group of formula -X-R^7 wherein:

- X is a direct bond, a C_1-C_4 alkylene group or a carbonyl group, for example, a direct bond or a C_1-C_4 alkylene group, wherein the C_1-C_4 alkylene group is unsubstituted or substituted by 1 or 2 substituents selected from phenyl, C_1-C_4 alkyl, hydroxy, -CO_2H and -CO_2-(C_1-C_4 alkyl) groups; and
- R^7 is a C_5-C_6 cycloalkyl group, a phenyl group or a cyclic group which is a 5- or 6- membered aromatic or non-aromatic ring which contains 1 or 2 heteroatoms selected from N, O and S and which is optionally fused to a phenyl ring, the phenyl

group being unsubstituted or substituted by 1 or 2 substituents selected from halogen atoms and C_1-C_4 alkyl, phenyl, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkythio, amino, mono- and di-(C_1-C_4 alkyl)amino and C_1-C_4 haloalkyl groups, and the cyclic group being unsubstituted or substituted by 1 or 2 substituents selected from halogen atoms and C_1-C_4 alkyl, phenyl, phenyl-(C_1-C_4-alkyl)-, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, amino, mono- and di-(C_1-C_4 alkyl)amino and C_1-C_4 haloalkyl groups,

provided that when X is substituted, R^7 is a said unsubstituted or substituted phenyl group.

Preferably, when R^{10} and R^{11} are as defined in option (c) above, R^{10} is hydrogen or a C_1-C_4 alkyl group and R^{11} is a group of formula -X-R^7 wherein:

- X is a direct bond, a C_1-C_4 alkylene group or a carbonyl group, for example, a direct bond or a C_1-C_4 alkylene group, wherein the C_1-C_4 alkylene group is unsubstituted or substituted by 1 or 2 substituents selected from C_1-C_4 alkyl, hydroxy, -CO_2H and -CO_2-(C_1-C_4 alkyl) groups; and

-R^7 is a cyclopentyl, cyclohexyl, benzimidazolyl, benzothiazolyl, thiadiazolyl, furanyl, thienyl, pyrimidinyl, pyrazinyl, isoxazolyl, pyrazolyl, pyridyl, phenyl or piperidinyl group, for example a cyclopentyl, cyclohexyl, benzimidazolyl, benzothiazolyl, thiadiazolyl, furanyl, pyridyl, phenyl or piperidinyl group, the pyridyl, pyrimidinyl, piperidinyl, thiadiazolyl and furanyl groups being unsubstituted or substituted by 1 or 2 substituents selected from halogen atoms and hydroxy, C_1-C_4 alkoxy, phenyl, phenyl-C_1-C_4 alkyl- and C_1-C_4 alkyl groups, and the phenyl, benzothiazolyl and benzimidazolyl groups being unsubstituted or substituted by 1 or 2 substituents selected from halogen atoms and hydroxy, C_1-C_4 alkoxy, and C_1-C_4 alkyl groups,

provided that when X is substituted, R^7 is an unsubstituted phenyl group.

Most preferably, when R^{10} and R^{11} are as defined in option (c) above, R^{10} is hydrogen or a C_1-C_4 alkyl group and R^{11} is a phenyl, pyridyl, thiadiazolyl, thienyl or phenylcarbonyl group, which is unsubstituted or substituted by one or two halogen atoms. In this embodiment, R^{11} is, for example, a phenyl, pyridyl or thiadiazolyl group.

Typically, when the substituents R^{16} and R^{17} form a said 4 to 8 membered ring, R^{16} and R^{17} are either on adjacent atoms or on the same atom. When R^{16} and R^{17} are on adjacent atoms, the said 4 to 8 membered ring is typically a phenyl ring. When R^{16} and R^{17} are on the same atom, the said 4 to 8 membered ring is typically a saturated 5- or 6-membered ring, for example a cyclohexyl ring or a piperidyl ring.

Typically, R^{14} to R^{17} are the same or different and each independently represents hydrogen, a halogen atom, a group of formula $-(CH_2)_n-R^7$ wherein n and R^7 are as defined above, or a C_1-C_6 alkyl group, for example hydrogen, a group of formula $-(CH_2)_n-R^7$ or a C_1-C_6 alkyl group or R^{14} and R^{15} are as defined above and R^{16} and R^{17}, together with the atoms to which they are attached, form a 4 to 8 membered aromatic or non-aromatic ring which contains from 0 to 4 heteroatoms selected from N, O and S and which is unsubstituted or substituted by 1 or 2 substituents selected from halogen atoms and C_1-C_6 alkyl, C_1-C_6 haloalkyl, hydroxy, phenyl, phenyl-(C_1-C_6 alkyl)-, amino and mono- and di-(C_1-C_6 alkyl)amino groups.

Preferably, R^{14} to R^{17} are the same or different and each independently represents hydrogen, a halogen atom, a 5- or 6- membered heteroaryl group having 1 or 2 heteroatoms selected from N, O and S, for example pyridyl, a C_1-C_4 alkyl group or a phenyl group which is unsubstituted or substituted by 1 or 2 substituents selected from halogen atoms, C_1-C_4 alkyl groups and C_1-C_4 haloalkyl groups. In this embodiment R^{14} to R^{17} are, for example, the same or different and each independently represents hydrogen, a 5- or 6-membered heteroaryl group, a C_{1-4} alkyl group or a phenyl group, which is unsubstituted or substituted as described above. Alternatively, R^{14} and R^{15} are as defined above and R^{16} and R^{17}, together with the atoms to which they are attached, form a 5- or 6- membered aromatic or non-aromatic ring which contains 0, 1 or 2 heteroatoms selected from N, O and S and which is unsubstituted or substituted by 1 or 2 substituents selected from C_1-C_4 alkyl, phenyl and phenyl-(C_1-C_4 alkyl)- substituents. More preferably, the 5- or 6- membered ring is a phenyl ring or a piperidylidene ring.

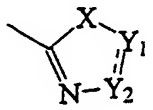
Typically, R^6 represents $-C(O)NR^{10}R^{11}$, wherein R^{10} and R^{11} are as defined above, $-ON=CR^{12}R^{13}$, wherein R^{12} and R^{13} are as defined above, or a phenyl,

heterocyclyl or heteroaryl group, for example a heterocyclyl or heteroaryl group, the phenyl, heterocyclyl and heteroaryl groups being unsubstituted or subsituted with substituents R^{14} to R^{17}, as defined above.

Typically, when R^6 is phenyl, it is unsubstituted or substituted by one halogen atom.

Typically, when R^6 is a heterocyclyl or heteroaryl group it is a 5- or 6-membered heterocyclyl or heteroaryl group, which group contains 1, 2 or 3 heteroatoms selected from N, O and S and is unsubstituted or substituted with substituents R^{14} to R^{17}, as defined above.

Preferably, the heterocyclyl or heteroaryl group is a 6- membered heteroaryl group having 1 or 2 heteroatoms selected from N, O and S, for example pyridyl, pyrimidinyl and pyrazinyl groups, or a group of formula (H)



(H)

wherein X represents O, S or N, and the $-Y_1=\!=\!=Y_2-$ moiety represents $-N=C(R^{18})-$, $-C(R^{18})=N-$, $-C(R^{18})=C(R^{19})-$ or $-CH(R^{18})-CH(R^{19})-$, wherein

R^{18} and R^{19} are the same or different and each represents hydrogen, a group of formula $-(CH_2)_n-R^7$ wherein n and R^7 are as defined above, or an alkyl group, the alkyl group being unsubstituted or substituted by one or more, for example 1 or 2, substituents selected from hydroxy, alkoxy, alkylthio, amino, mono- and di-alkylamino, hydroxycarbonyl, alkoxycarbonyl, acylamino, carbamoyl, alkylcarbamoyl, dihydroxyphosphoryloxy, dialkoxyphosphoryloxy and haloalkyl groups, or R^{18} and R^{19}, together with the atoms to which they are attached, form a 4 to 8 membered, aromatic or non-aromatic ring, which contains from 0 to 4 heteroatoms selected from N, O and S and which is unsubstituted or substituted by one or more, for example 1 or 2, substituents selected from halogen atoms and alkyl, hydroxy, phenyl, alkoxycarbonyl,

amino, mono-alkylamino, di-alkylamino and hydroxycarbonyl groups, the alkyl substituents being unsubstituted or substituted by one or more, for example 1 or 2, further substituents selected from halogen atoms and hydroxy, alkoxy, alkylthio, acylamino, carbamoyl, alkylcarbamoyl, dihydroxyphosphoryloxy, dialkoxyphosphoryloxy, hydroxyalkoxy, phenyl, alkoxycarbonyl, amino, mono- and di-alkylamino and hydroxycarbonyl groups.

Typically, when R^{18} and R^{19} form a said 4 to 8 membered ring, R^{18} and R^{19} are either on adjacent atoms or on the same atom. When R^{18} and R^{19} are on adjacent atoms, the said 4 to 8 membered ring is typically a phenyl ring. When R^{18} and R^{19} are on the same atom, the said 4 to 8 membered ring is typically a saturated 5- or 6- membered ring, for example a cyclohexyl ring or a piperidyl ring.

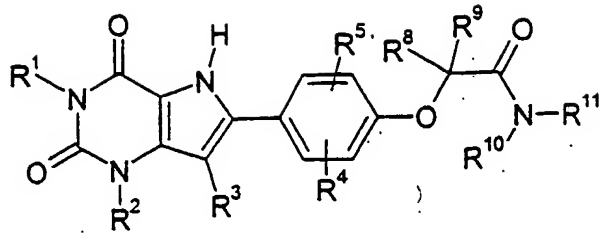
Typically, R^{18} and R^{19} are the same or different and each independently represents hydrogen, a group of formula $-(CH_2)_n-R^7$ wherein n and R^7 are as defined above, or a C_1-C_6 alkyl group, or R^{18} or R^{19}, together with the atoms to which they are attached, form a 4 to 8 membered aromatic or non-aromatic ring which contains from 0 to 4 heteroatoms selected from N, O and S and which is unsubstituted or substituted by 1 or 2 substituents selected from halogen atoms and C_1-C_6 alkyl, C_1-C_6 haloalkyl, hydroxy, phenyl, phenyl-C_1-C_6 alkyl, amino and mono- and di-(C_1-C_6 alkyl)amino groups.

Preferably, R^{18} and R^{19} are the same or different and each independently represent hydrogen, a 5- or 6- membered heteroaryl group having 1 or 2 heteroatoms selected from N, O and S, for example pyridyl, a C_1-C_4 alkyl group or a phenyl group which is unsubstituted or substituted by 1 or 2 substituents selected from halogen atoms, C_1-C_4 alkyl groups and C_1-C_4 haloalkyl groups, or R^{18} and R^{19}, together with the atoms to which they are attached, form a 5- or 6- membered aromatic or non aromatic ring which contains 0, 1 or 2 heteroatoms selected from N, O and S and which is unsubstituted or substituted by 1 or 2 substitutents selected from C_1-C_4 alkyl, phenyl and phenyl-(C_1-C_4 alkyl)- substituents.

Preferably, R^6 represents $-C(O)NR^{10}R^{11}$, wherein R^{10} and R^{11} are as defined above, $-ON=CR^{12}R^{13}$ wherein R^{12} and R^{13} are as defined above, a phenyl group which is optionally substituted by a halogen atom, or a 5- or 6- membered heteroaryl or heterocyclyl group which is optionally fused to a phenyl ring and which is unsubstituted or substituted by 1 or 2 substituents selected from phenyl, pyridyl, phenyl-(C_1-C_4 alkyl)-, C_1-C_4 alkyl and piperidylidene substituents, the phenyl subsitutents being unsubstiuted or substituted by 1 or 2 further substituents selected from halogen atoms and C_1-C_4 alkyl groups and the piperidylidene substituents being unsubstituted or substituted by 1 or 2 further substituents selected from phenyl, phenyl-(C_1-C_4 alkyl)- and C_1-C_4 alkyl groups.

More preferably, R^6 represents $-C(O)NR^{10}R^{11}$, a phenyl group or an oxadiazolyl group, for example a group $-C(O)NR^{10}R^{11}$ or an oxadiazolyl group, wherein the oxadiazolyl group is unsubstituted or substituted by a phenyl group wherein either R^{10} is hydrogen and R^{11} is a thiadiazolyl group, a pyridyl group, a phenyl group, a thienyl group or a phenylcarbonyl group, for example a thiadiazolyl group, a pyridyl group or a phenyl group, the thiadiazolyl, pyridyl, phenyl, thienyl and phenylcarbonyl groups being unsubstituted or substituted by 1 or 2 substituents selected from halogen atoms and phenyl and benzyloxy groups or R^{10} and R^{11} form, together with the N atom to which they are attached, a 1, 2, 3, 4-tetrahydroisoquinoline group, a 1,3,4,9-tetrahydro-beta-carbolinyl group, a piperidine group or a piperazine group, for example a 1, 2, 3, 4-tetrahydroisoquinoline group, a piperidine group or a piperazine group, the piperidine and piperazine groups being unsubstituted or substituted by 1 or 2 substituents selected from phenyl, pyridyl and hydroxy groups, the phenyl and pyridyl groups being optionally further substituted by one or two halogen atoms, for example chlorine atoms. The piperidine and piperazine groups are, for example, substituted by one or two phenyl groups.

Preferred compounds of formula I include the compounds of formula Ia described hereinbelow, and pharmaceutically acceptable salts thereof:



Ia

wherein R^1, R^2, R^3, R^4, R^5, R^8, R^9, R^{10} and R^{11} are as defined above.

Preferably, in the formulae (I) and (IA),

- R^1 and R^2 are the same or different and each independently represent hydrogen, a group of formula $-(CH_2)_n-R^7$ wherein n and R^7 are as defined above or a C_1-C_6 alkyl group which is unsubstituted or substituted by one or more, for example 1 or 2, substituents selected from hydroxy, C_1-C_6 alkoxy, C_1-C_6 alkylthio, amino, and mono- and di-(C_1-C_6alkyl)amino groups.
- R^3 represents hydrogen, halogen or a C_1-C_6 alkyl group which is unsubstituted or substituted by one or more, for example 1 or 2, substituents selected from halogen atoms and hydroxy groups;
- R^4 and R^5 are the same or different and each represent hydrogen, halogen, C_1-C_6 alkyl, C_1-C_6 haloalkyl, hydroxy, C_1-C_6 alkoxy, C_1-C_6 alkylthio, amino or mono- or di-(C_1-C_6 alkyl)amino.

Preferably, L_1 is a direct bond or $-O(CH_2)_m-$, $-O(CR^8R^9)_m-$, $-S(CR^8R^9)_m-$, $-CH=CH-$, $-(CH_2)_m-$, $-(CR^8R^9)_m-$, $-(CH_2)_mO-$, $-(CR^8R^9)_mO-$, $-O(CH_2)_mO-$, $-(CR^8R^9)_mN(Z)-$ or $-N(Z)(CR^8R^9)_m-$, for example, a direct bond or $-O(CH_2)_m-$, $-O(CR^8R^9)_m-$, $-S(CR^8R^9)_m-$, $-CH=CH-$, $-(CH_2)_m-$, $-(CR^8R^9)_m-$, $-(CH_2)_mO-$, $-(CR^8R^9)_mO-$, $-(CR^8R^9)_mN(Z)-$ or $-N(Z)(CR^8R^9)_m-$, wherein m is from 1 to 4, Z is hydrogen or C_1-C_4 alkyl and R^8 and R^9 are the same or different and each represent hydrogen, C_1-C_4 alkyl, C_3-C_6 cycloalkyl, (C_3-C_6 cycloalkyl)-(C_1-C_4 alkyl)-, phenyl or phenyl-(C_1-C_4 alkyl)-; and

- R^6 represents $-C(O)NR^{10}R^{11}$, $-ON=CR^{12}R^{13}$, or a phenyl, heterocyclyl or heteroaryl group, for example a heterocyclyl or heteroaryl group, the phenyl, heterocyclyl and heteroaryl groups being unsubstituted or substituted with substituents R^{14} to R^{17}, wherein:

R^{10} and R^{11} are either:

(a) the same or different, each independently representing hydrogen, a C_1-C_6 alkyl group, a C_3-C_6 cycloalkyl group optionally fused to a phenyl ring, or a phenyl group, the alkyl group being unsubstituted or substituted by 1 or 2 substituents selected from hydroxy, halogen, C_1-C_4 alkoxy and amino groups and the phenyl and cycloalkyl groups being unsubstituted or substituted by 1, 2, 3 or 4 substitutents selected from (1) groups of formula $-(CH_2)_nR^7$, $-O-(CH_2)_nR^7$, $-S-(CH_2)_n-R^7$ and -COR and -CONHR wherein R is C_1-C_6 alkyl or $-(CH_2)_nR^7$ and n and R^7 are as defined above, (2) groups of formula $-(CH_2)_n-S(O)_2NR'R''$ wherein n is as defined above and R' and R'' are the same or different and are each selected from hydrogen and C_1-C_6 alkyl or form, together with the N atom to which they are attached, a 4- or 5- membered saturated heterocyclic ring containing 1 or 2 heteroatoms selected from N, O and S, (3) groups of formula $-(CH_2)_n-CO_2R'''$ wherein n is as defined above and R''' is hydrogen or C_1-C_6 alkyl, (4) groups of formula $-N^+R''''_3$ wherein each R'''' is the same or different and is a C_1-C_6 alkyl group, and (5) halogen atoms and C_1-C_6 alkyl, hydroxy, C_1-C_4 alkylenedioxy, C_1-C_6 alkoxy, C_1-C_6 alkylthio, amino, mono- and di-(C_1-C_6 alkyl)amino, nitro, cyano, hydroxycarbonyl, (C_1-C_6 alkoxy)carbonyl, (C_1-C_7 acyl)amino, carbamoyl and C_1-C_6 haloalkyl groups,

(b) together with the N atom to which they are attached, a 3- to 7- membered ring containing from 1 to 4 heteroatoms selected from N, O and S which ring is (i) optionally fused to an aromatic ring or to a heteroaromatic ring which is in turn optionally fused to an aromatic ring and is (ii) substituted or unsubstituted by 1, 2 or 3 substituents independently selected from halogen atoms, groups of formula $-X-R^7$ and $-CO_2-X-R^7$ wherein X is a direct bond, a C_1-C_4 alkylene group or a carbonyl group, for example a direct bond or a C_1-C_4 alkylene group and R^7 is as defined above, and hydroxy, cyano, nitro, carbamoyl, hydroxycarbonyl, C_1-C_6 alkoxycarbonyl, mono- and di-(C_1-C_6 alkyl)amino, amino, divalent alkylene and C_1-C_6 alkyl groups, the alkyl substituents being unsubstituted or substituted by 1 or 2 further substituents selected from hydroxy and amino groups and the moiety X being unsubstituted or substituted by

one or two substituents selected from phenyl, C_1-C_4 alkyl, hydroxy, -CO_2H and -CO_2-(C_1-C_4 alkyl), or

(c) defined so that R^{10} is hydrogen or a C_1-C_4 alkyl group and R^{11} is a group of formula -X'-$R^{7'}$ wherein:

- X' is a direct bond, a C_1-C_4 alkylene group or a carbonyl group, for example a direct bond or a C_1-C_4 alkylene group, wherein the C_1-C_4 alkylene group is unsubstituted or substituted by 1 or 2 substituents selected from phenyl, C_1-C_4 alkyl, hydroxy, -CO_2H and -CO_2-(C_1-C_4 alkyl) groups; and
- $R^{7'}$ is a C_5-C_6 cycloalkyl group, a phenyl group or a cyclic group which is a 5- or 6- membered aromatic or non-aromatic ring which contains 1 or 2 heteroatoms selected from N, O and S and which is optionally fused to a phenyl ring, the phenyl group being unsubstituted or substituted by 1 or 2 substituents selected from halogen atoms and C_1-C_4 alkyl, phenyl, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, amino, mono- and di-(C_1-C_4 alkyl) amino and C_1-C_4 haloalkyl groups, and the cyclic group being unsubstituted or substituted by 1 or 2 substituents selected from halogen atoms and C_1-C_4 alkyl, phenyl, phenyl-(C_1-C_4-alkyl)-, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, amino, mono- and di-(C_1-C_4 alkyl)amino and C_1-C_4 haloalkyl groups,

provided that when X' is substituted, $R^{7'}$ is a said unsubstituted or substituted phenyl group,

R^{12} and R^{13} are the same or different and each represent hydrogen, amino, (C_1-C_6 alkyl)amino, di-(C_1-C_6 alkyl)amino, C_1-C_6 alkyl, C_3-C_6 cycloalkyl or phenyl, the alkyl moieties being unsubstituted or substituted by 1 or 2 substitutents selected from hydroxy groups and halogen atoms and the cycloalkyl group and the phenyl group being unsubstituted or substituted by 1, 2, 3 or 4 substituents selected from halogen atoms and C_1-C_4 alkoxy, C_1-C_4 alkylthio, C_1-C_4 alkyl, hydroxy, C_1-C_4 haloalkyl, amino, and mon- and di-(C_1-C_4 alkyl)amino groups, and

R^{14} to R^{17} are the same or different and each independently represent hydrogen, a halogen atom, a group of formula -$(CH_2)_n$-R^7 wherein n and R^7 are as defined above, or a C_1-C_6 alkyl group, for example hydrogen, a group of formula -$(CH_2)_n$-R^7 or a C_1-C_6

alkyl group, or R^{14} and R^{15} are as defined above and R^{16} and R^{17}, together with the atoms to which they are attached, form a 4 to 8 membered aromatic or non-aromatic ring which contains from 0 to 4 heteroatoms selected from N, O and S and which is unsubstituted or substituted by 1 or 2 substituents selected from halogen atoms and C_1-C_6 alkyl, C_1-C_6 haloalkyl, hydroxy, phenyl, phenyl-(C_1-C_6 alkyl)-, amino and mono- and di-(C_1-C_6 alkyl)amino groups.

Particular individual compounds of the invention include:

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-phenylacetamide

6-{4-[2-Oxo-2-(4-phenylpiperazin-1-yl)ethoxy]phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(4-fluorophenyl) acetamide

6-{4-[2-(3,4-Dihydro-1*H*-isoquinolin-2-yl)-2-oxoethoxy] phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

N-(4-Chlorophenyl)-2-[4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] acetamide

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy]-*N*-(4-trifluoro methoxyphenyl)acetamide

N-(4-Cyanophenyl)-2-[4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] acetamide

4-{2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]acetylamino}benzamide

6-{4-[2-Oxo-2-(2,3,5,6-tetrahydro-[1,2']bipyrazinyl-4-yl)ethoxy]phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(4-methoxyphenyl) acetamide

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-*p*-tolylacetamide

N-(4-Acetylphenyl)-2-[4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] acetamide

4-{2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]acetylamino}benzoic acid ethyl ester

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(4-trifluoromethyl phenyl)acetamide

6-(4-{2-[4-(2-Chlorophenyl)piperazin-1-yl]-2-oxo-ethoxy}phenyl)-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione

N-(4-*tert*-Butylphenyl)-2-[4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] acetamide

1-{2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]acetyl}-4-phenyl-piperidine-4-carbonitrile

6-{4-[2-(4-Benzhydrylpiperazin-1-yl)-2-oxoethoxy] phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(2-hydroxy-1-phenylethyl)acetamide

N-(2-Chloro-1-phenylethyl)-2-[4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy]acetamide

N-(4-Benzoylphenyl)-2-[4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] acetamide

N-(4-Cyanomethylphenyl)-2-[4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] acetamide

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(4-sulfamoylphenyl) acetamide

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(4-hydroxy-phenyl)acetamide

N-Biphenyl-4-yl-2-[4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] acetamide

N-(4-Benzyloxyphenyl)-2-[4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] acetamide

4-{2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]acetyl}piperazine-1-carboxylic acid benzyl ester

4-{2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]acetylamino}-*N*-[2-(4-methoxyphenyl)ethyl]benzamide

4-{2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]acetyl}piperazine-1-carboxylic acid phenyl ester

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-[4-(pyrrolidine-1-sulfonylmethyl)phenyl]acetamide

6-{4-[2-(4,4-Diphenyl-piperidin-1-yl)-2-oxo-ethoxy] phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-(4-{2-[4-(4-Methoxyphenyl)piperidin-1-yl]-2-oxo-ethoxy}phenyl)-1,3-dipropyl-1,5-dihydro-pyrrolo[3,2-*d*] pyrimidine-2,4-dione

(4-{2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]acetylamino}phenyl) acetic acid ethyl ester

6-(4-{2-[4-(1-Methyl-1*H*-benzoimidazol-2-ylmethyl)piperazin-1-yl]-2-oxoethoxy}phenyl)-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[2-(3,3-Diphenylpiperazin-1-yl)-2-oxo-ethoxy]phenyl}-1,3-dipropyl-1,5-dihydro-pyrrolo[3,2-*d*] pyrimidine-2,4-dione

N-[4-(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)phenyl]-2-[4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]acetamide

(4-{2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]acetylamino} phenyl)trimethyl ammonium

6-(4-{2-[4-(3,5-Dichloropyridin-4-yl)piperazin-1-yl]-2-oxo-ethoxy}-phenyl)-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-(4-{2-[4-(6-Chlorobenzothiazol-2-yl)piperazin-1-yl]-2-oxo-ethoxy}phenyl)-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione

N-(4-Acetylaminophenyl)-2-[4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] acetamide

6-{4-[2-Oxo-2-(1,3,4,9-tetrahydro-β-carbolin-2-yl)ethoxy]phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(4-iodophenyl) acetamide

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(2-hydroxy-2-phenylethyl)acetamide

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy]-*N*-(2-hydroxy-1-methyl-2-phenylethyl)acetamide

N-(7-Cyano-3-hydroxy-2,2-dimethylchroman-4-yl)-2-[4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy]acetamide

N-(1-Benzyl-3-hydroxypiperidin-3-ylmethyl)-2-[4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy]acetamide

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy]-*N*-[2-hydroxy-2-(4-hydroxyphenyl)ethyl]acetamide

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy]-*N*-[2-hydroxy-2-(4-hydroxy-3-hydroxymethylphenyl)ethyl]acetamide

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy]-*N*-(2-hydroxyindan-1-yl)acetamide

6-{4-[2-Oxo-2-(6-*o*-tolyl-2,6-diazabicyclo[2.2.1]hept-2-yl)ethoxy]phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy]-*N*-(2-hydroxyphenyl) acetamide

{2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy]acetylamino} phenylacetic acid methyl ester

{2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy]acetylamino} phenylacetic acid

(4-{2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy]acetylamino} phenyl)acetic acid

N-(2-Aminoethyl)-2-[4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] acetamide

N-(4-Bromophenyl)-2-[4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] acetamide

2-[4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-phenylacetamide

2-[4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(4-fluorophenyl) acetamide

1,3-Dimethyl-6-{4-[2-(4-methylpiperazin-1-yl)-2-oxo-ethoxy]phenyl}-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

1,3-Dimethyl-6-[4-(2-morpholin-4-yl-2-oxoethoxy)phenyl]-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[2-(3,4-Dihydro-1*H*-isoquinolin-2-yl)-2-oxoethoxy] phenyl}-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

N-Cyclopentyl-2-[4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] acetamide

N-(4-Acetylphenyl)-2-[4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] acetamide

N-(1*H*-Benzoimidazol-2-yl)-2-[4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl) phenoxy]acetamide

N-(4-Cyanophenyl)-2-[4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] acetamide

6-{4-[2-(3,4-Dihydro-2*H*-quinolin-1-yl)-2-oxoethoxy] phenyl}-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

2-[4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-[1,3,4]thiadiazol-2-ylacetamide

1,3-Dimethyl-6-{4-[2-oxo-2-(4-phenylpiperazin-1-yl)ethoxy]phenyl}-1,5-

dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

2-[4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(4-nitrophenyl) acetamide

6-(4-{2-[4-(4-Fluorophenyl)piperazin-1-yl]-2-oxoethoxy}phenyl)-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione

6-{4-[2-(4-Benzylpiperazin-1-yl)-2-oxoethoxy]phenyl}-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-(4-{2-[4-(2-Methoxyphenyl)piperazin-1-yl]-2-oxoethoxy} phenyl)-1,3-dimethyl-1,5-dihydro-pyrrolo[3,2-*d*] pyrimidine-2,4-dione

6-(4-{2-[4-(4-Methoxyphenyl)piperazin-1-yl]-2-oxo ethoxy}phenyl)-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione

1,3-Dimethyl-6-(4-{2-oxo-2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethoxy}phenyl)-1,5-dihydropyrrolo [3,2-*d*]pyrimidine-2,4-dione

1,3-Dimethyl-6-{4-[2-oxo-2-(4-pyridin-2-yl-piperazin-1-yl)ethoxy]phenyl}-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

1,3-Dimethyl-6-{4-[2-oxo-2-(4-pyrimidin-2-ylpiperazin-1-yl)ethoxy]phenyl}-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

N-Benzyl-2-[4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-methylacetamide

N-Benzyl-2-[4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-ethylacetamide

2-[4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy]-*N*-indan-1-yl-acetamide

2-[4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy]-*N*-(4-fluorobenzyl) acetamide

2-[4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy]-*N*-furan-2-ylmethyl acetamide

N-(4-Chlorobenzyl)-2-[4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy] acetamide

2-[4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-d]pyrimidin-6-yl)-phenoxy]-*N*-(1-phenylethyl) acetamide

2-[4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy]-*N*-(3-methoxybenzyl) acetamide

N-Benzyl-2-[4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy] acetamide

1,3-Dimethyl-6-{4-[4-oxo-4-(6-*o*-tolyl-2,6-diazabicyclo[2.2.1]hept-2-yl)butoxy]phenyl}-1,5-dihydropyrrolo[3,2-d] pyrimidine-2,4-dione

2-[4-(1,3-Diethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-phenylacetamide

1,3-Diethyl-6-{4-[2-oxo-2-(4-phenylpiperazin-1-yl)ethoxy]phenyl}-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

N-(4-Cyanophenyl)-2-[4-(1,3-diethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy] acetamide

2-[4-(1-Methyl-2,4-dioxo-3-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-phenylacetamide

N-(4-Fluorophenyl)-2-[4-(1-methyl-2,4-dioxo-3-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] acetamide

N-(4-Chlorobenzyl)-2-[4-(1-methyl-2,4-dioxo-3-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] acetamide

6-{4-[2-(3,4-Dihydro-1*H*-isoquinolin-2-yl)-2-oxo-ethoxy]phenyl}-1-methyl-3-propyl-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione

1-Methyl-6-{4-[2-oxo-2-(4-phenyl-piperazin-1-yl) ethoxy]phenyl}-3-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-(4-{2-[4-(4-Fluorophenyl)piperazin-1-yl]-2-oxo-ethoxy}phenyl)-1-methyl-3-propyl-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione

4-{2-[4-(1-Methyl-2,4-dioxo-3-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] acetylamino}benzoic acid ethyl ester

6-{4-[2-(4-Hydroxy-4-phenylpiperidin-1-yl)-2-oxo ethoxy]phenyl}-1-methyl-3-

propyl-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione

1-{2-[4-(1-Methyl-2,4-dioxo-3-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]acetyl}-4-phenylpiperidine-4-carbonitrile

N-Biphenyl-4-yl-2-[4-(1-methyl-2,4-dioxo-3-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] acetamide

6-{4-[2-(4,4-Diphenylpiperidin-1-yl)-2-oxo-ethoxy] phenyl}-1-methyl-3-propyl-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione

6-(4-{2-[4-(4-Methoxyphenyl)piperidin-1-yl]-2-oxo-ethoxy}phenyl)-1-methyl-3-propyl-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione

(4-{2-[4-(1-Methyl-2,4-dioxo-3-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] acetylamino}phenyl)acetic acid ethyl ester

6-{4-[2-(3,3-Diphenylpiperazin-1-yl)-2-oxoethoxy] phenyl}-1-methyl-3-propyl-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione

6-(4-{2-[4-(6-Chlorobenzothiazol-2-yl)-piperazin-1-yl]-2-oxoethoxy}phenyl)-1-methyl-3-propyl-1,5-dihydro pyrrolo[3,2-*d*]pyrimidine-2,4-dione

1-Methyl-6-{4-[2-oxo-2-(1,3,4,9-tetrahydro-β-carbolin-2-yl)ethoxy]phenyl}-3-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

N-(4-Iodophenyl)-2-[4-(1-methyl-2,4-dioxo-3-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] acetamide

1-Methyl-6-{4-[4-oxo-4-(6-*o*-tolyl-2,6-diazabicyclo[2.2.1]hept-2-yl)butoxy]phenyl}-3-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

N-(4-Fluorophenyl)-2-[4-(3-methyl-2,4-dioxo-1-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] acetamide

2-[4-(3-Methyl-2,4-dioxo-1-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-phenylacetamide

N-(4-Bromophenyl)-2-[4-(3-methyl-2,4-dioxo-1-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] acetamide

6-{4-[2-(3,4-Dihydro-1*H*-isoquinolin-2-yl)-2-oxoethoxy] phenyl}-3-methyl-1-propyl-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione

N-Benzyl-2-[4-(3-methyl-2,4-dioxo-1-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy] acetamide

N-Benzyl-*N*-methyl-2-[4-(3-methyl-2,4-dioxo-1-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] acetamide

3-Methyl-6-{4-[2-oxo-2-(4-phenylpiperazin-1-yl)-ethoxy]phenyl}-1-propyl-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione

6-{4-[2-(4-Benzylpiperazin-1-yl)-2-oxoethoxy]phenyl}-3-methyl-1-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

3-Methyl-6-{4-[4-oxo-4-(6-*o*-tolyl-2,6-diazabicyclo[2.2.1]hept-2-yl)butoxy]phenyl}-1-propyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

N-Cyclopentyl-2-{4-[1-(3-methoxypropyl)-3-methyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl] phenoxy}acetamide

2-{4-[1-(3-Methoxypropyl)-3-methyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl]phenoxy}-*N*-phenylacetamide

2-[4-(3-Isobutyl-1-methyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-phenylacetamide

3-Isobutyl-1-methyl-6-{4-[2-oxo-2-(4-phenylpiperazin-1-yl)ethoxy]phenyl}-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

4-{2-[4-(2,4-Dioxo-1-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]acetylamino}benzoic acid ethyl ester

6-(4-{2-[4-(4-Methoxyphenyl)piperidin-1-yl]-2-oxo-ethoxy}phenyl)-1-propyl-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione

6-(4-{2-[4-(4-Methoxyphenyl)piperazin-1-yl]-2-oxo-ethoxy}phenyl)-1-propyl-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione

N-(4-Bromophenyl)-2-[4-(2,4-dioxo-1-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] acetamide

2-[4-(2,4-Dioxo-1-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(4-fluorophenyl) acetamide

2-{4-[1,3-Bis(2-methoxyethyl)-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-

d]pyrimidin-6-yl]phenoxy}-*N*-phenylacetamide

2-{4-[1,3-Bis(2-methoxyethyl)-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-d]pyrimidin-6-yl]phenoxy}-*N*-(4-fluorophenyl)acetamide

2-{4-[1,3-Bis(2-methoxyethyl)-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl]phenoxy}-*N*-(4-bromophenyl)acetamide

1,3-Bis(2-methoxyethyl)-6-{4-[2-oxo-2-(4-phenylpiperazin-1-yl)ethoxy]phenyl}-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[2-(3,4-Dihydro-1*H*-isoquinolin-2-yl)-2-oxoethoxy]phenyl}-1,3-bis(2-methoxyethyl)-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione

2-[4-(1,3-Bis(cyclopropylmethyl)-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-phenylacetamide

2-[4-(1,3-Bis(cyclopropylmethyl)-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(4-fluorophenyl)acetamide

2-[4-(1,3-Bis(cyclopropylmethyl)-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(4-bromophenyl)acetamide

1,3-Bis(cyclopropylmethyl)-6-{4-[2-oxo-2-(4-phenylpiperazin-1-l)ethoxy]phenyl}-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione

1,3-Bis(cyclopropylmethyl)-6-{4-[2-(3,4-dihydro-1*H*-isoquinolin-2-yl)-2-oxoethoxy]phenyl}-1,5-dihydropyrrolo [3,2-*d*]pyrimidine-2,4-dione

2-[4-(7-Chloro-1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(4-cyanophenyl)acetamide

2-[4-(7-Bromo-2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-phenylacetamide

2-[4-(7-Bromo-2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(4-fluorophenyl)acetamide

2-[4-(7-Chloro-2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(4-fluorophenyl)acetamide

2-[4-(7-Chloro-2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-phenylacetamide

N-(4-Bromophenyl)-2-[4-(7-chloro-2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]acetamide

2-[4-(7-Chloro-2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(2-chlorophenyl)acetamide

2-[4-(7-Chloro-2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(4-chlorophenyl)acetamide

2-[4-(7-Chloro-2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(2-fluorophenyl)acetamide

2-[4-(7-Chloro-2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy]-*N*-(4-fluorobenzyl)acetamide

2-[4-(7-Chloro-2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(4-methoxyphenyl)acetamide

N-Benzyl-2-[4-(7-chloro-2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] acetamide

2-[4-(7-Chloro-2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-*p*-tolylacetamide

2-[4-(7-Chloro-2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(3-fluorophenyl)acetamide

2-[4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-3-methoxyphenoxy]-*N*-phenyl-acetamide

2-[4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-3-methoxy-phenoxy]-*N*-(4-fluorophenyl)acetamide

N-(4-Chlorobenzyl)-2-[4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-3-methoxyphenoxy]acetamide

6-{4-[2-(3,4-Dihydro-1*H*-isoquinolin-2-yl)-2-oxo-ethoxy]-2-methoxyphenyl}-1,3-dimethyl-1,5-dihydropyrrolo [3,2-*d*]pyrimidine-2,4-dione

6-{2-Methoxy-4-[2-oxo-2-(4-phenylpiperazin-1-yl)ethoxy]phenyl}-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione

N-(4-Cyanophenyl)-2-[4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-

pyrrolo[3,2-*d*]pyrimidin-6-yl)-3-methoxyphenoxy]acetamide

N-(4-Bromophenyl)-2-[4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-3-methoxyphenoxy]acetamide

6-(2-Methoxy-4-{2-[4-(4-methoxyphenyl)-piperidin-1-yl]-2-oxoethoxy}phenyl)-1,3-dimethyl-1,5-dihydropyrrolo [3,2-*d*]pyrimidine-2,4-dione

6-(2-Methoxy-4-{2-[4-(4-methoxyphenyl)-piperazin-1-yl]-2-oxoethoxy}phenyl)-1,3-dimethyl-1,5-dihydropyrrolo [3,2-*d*]pyrimidine-2,4-dione

2-[4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-2-methoxyphenoxy]-*N*-phenyl acetamide

2-[4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-2-methoxyphenoxy]-*N*-(4-fluorophenyl)acetamide

N-(4-Chlorobenzyl)-2-[4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-2-methoxyphenoxy-acetamide

6-{4-[2-(3,4-Dihydro-1*H*-isoquinolin-2-yl)-2-oxoethoxy] -3-methoxyphenyl}-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione

6-{3-Methoxy-4-[2-oxo-2-(4-phenylpiperazin-1-yl) ethoxy]phenyl}-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione

N-(4-Cyanophenyl)-2-[4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-2-methoxyphenoxy]acetamide

N-(4-Bromophenyl)-2-[4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-2-methoxyphenoxy]acetamide

4-{2-[4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-2-methoxyphenoxy] acetylamino}benzoic acid ethyl ester

6-(3-Methoxy-4-{2-[4-(4-methoxyphenyl)piperidin-1-yl]-2-oxoethoxy}phenyl)-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione

6-(3-Methoxy-4-{2-[4-(4-methoxyphenyl)piperazin-1-yl]-2-oxoethoxy}phenyl)-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy]-*N*-phenylpropionamide

6-{4-[2-(3,4-Dihydro-1*H*-isoquinolin-2-yl)-1-methyl-2-oxoethoxy]phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione

6-{4-[1-Methyl-2-oxo-2-(4-phenylpiperazin-1-yl)ethoxy]phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

N-(4-Chlorobenzyl)-2-[4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl) phenoxy]propionamide

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(4-fluorophenyl) propionamide

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(4-methoxyphenyl) propionamide

2-[4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-phenylpropionamide

2-[4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(4-fluorophenyl) propionamide

N-(4-Bromophenyl)-2-[4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] propionamide

1,3-Dimethyl-6-{4-[1-methyl-2-oxo-2-(4-phenyl piperazin-1-yl)ethoxy]phenyl}-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione

6-{4-[2-(3,4-Dihydro-1*H*-isoquinolin-2-yl)-1-methyl-2-oxoethoxy]phenyl}-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-phenylbutyramide

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(4-fluorophenyl) butyramide

N-(4-Bromophenyl)-2-[4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] butyramide

6-{4-[1-(4-Phenylpiperazine-1-carbonyl)propoxy]phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[1-(3,4-Dihydro-1*H*-isoquinoline-2-carbonyl) propoxy]phenyl}-1,3-

dipropyl-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-2-methyl-*N*-phenyl propionamide

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(4-fluorophenyl)-2-methylpropionamide

N-(4-Bromophenyl)-2-[4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] -2-methylpropionamide

6-{4-[1,1-Dimethyl-2-oxo-2-(4-phenylpiperazin-1-yl)ethoxy]phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione

6-{4-[2-(3,4-Dihydro-1*H*-isoquinolin-2-yl)-1,1-dimethyl -2-oxoethoxy]phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy]-2,*N*-diphenylacetamide

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(4-fluorophenyl)-2-phenylacetamide

6-{4-[2-Oxo-1-phenyl-2-(4-phenylpiperazin-1-yl)ethoxy] phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

3-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenyl]-*N*-phenylpropionamide

3-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenyl]-*N*-(4-fluorophenyl) propionamide

6-{4-[3-Oxo-3-(4-phenylpiperazin-1-yl)propyl]phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[3-(3,4-Dihydro-1*H*-isoquinolin-2-yl)-3-oxopropyl] phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

3-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenyl]-*N*-phenylacrylamide

6-{4-[3-Oxo-3-(4-phenylpiperazin-1-yl)propenyl]phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[3-(3,4-Dihydro-1*H*-isoquinolin-2-yl)-3-oxo propenyl]phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione

4-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-phenylbutyramide

4-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(4-fluorophenyl) butyramide

6-{4-[4-Oxo-4-(4-phenylpiperazin-1-yl)butoxy]phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-(3,4-Dihydro-1*H*-isoquinolin-2-yl)-4-oxobutoxy] phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[4-Oxo-4-(6-*o*-tolyl-2,5-diazabicyclo[2.2.1]hept-2-yl)butoxy]phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione

4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-phenylbenzamide

4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-*N*-(4-fluorophenyl)benzamide

N-(4-Bromophenyl)-4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzamide

6-[4-(4-Phenylpiperazine-1-carbonyl)phenyl]-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-[4-(3,4-Dihydro-1*H*-isoquinoline-2-carbonyl)phenyl]-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-[4-(3-Phenyl-[1,2,4]oxadiazol-5-ylmethoxy)phenyl]-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[2-oxo-2-{[amino(4-fluorophenyl)methylene diamino]oxy}ethoxy]phenyl}-1,3-dipropyl-1,5-dihydropyrrolo [3,2-*d*]pyrimidine-2,4-dione

6-{4-[3-(4-Fluorophenyl)-[1,2,4]oxadiazol-5-ylmethoxy] phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

1,3-Dipropyl-6-[4-(3-pyridin-4-yl-[1,2,4]oxadiazol-5-ylmethoxy)phenyl]-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-[4-(Benzooxazol-2-ylmethoxy)phenyl]-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-[4-(5-Phenyl-4,5-dihydrooxazol-2-ylmethoxy)phenyl]-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-[4-(4-Methyl-5-phenyl-4,5-dihydrooxazol-2-ylmethoxy)phenyl]-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-[4-(7-Benzyl-1-oxa-3,7-diazaspiro[4.5]dec-2-en-2-ylmethoxy)phenyl]-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

1,3-Dipropyl-6-[4-(quinolin-2-ylmethoxy)phenyl]-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy]-N-pyridin-2-ylacetamide

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy]-N-(3-hydroxypyridin-2-yl)acetamide

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)-phenoxy]-N-(5-methylpyridin-2-yl)acetamide

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)-phenoxy]-N-pyridin-3-ylacetamide

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)-phenoxy]-N-(6-methoxypyridin-3-yl)acetamide

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy]-N-pyridin-4-ylmethylacetamide

6-(4-{2-Oxo-2-[4-(4-trifluoromethylphenyl)piperazin-1-yl]ethoxy}phenyl)-1,3-dipropyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

6-(4-{2-[4-(3-Chlorophenyl)piperazin-1-yl]-2-oxoethoxy}phenyl)-1,3-dipropyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)-phenoxy]-N-pyrazin-2-ylacetamide

N-(2,6-Dimethoxypyrimidin-4-yl)-2-[4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy]acetamide

6-{4-[2-(3-Aminopyrazol-1-yl)-2-oxoethoxy]phenyl}-1,3-dipropyl-1,5-dihydro-pyrrolo[3,2-d]pyrimidine-2,4-dione

6-(4-{2-[4-(3-Chlorophenyl)piperazin-1-yl]-2-oxoethoxy}phenyl)-1,3-dimethyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

1,3-Dimethyl-6-(4-{2-oxo-2-[4-(4-trifluoromethylphenyl)piperazin-1-yl]ethoxy}phenyl)-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

6-(4-{2-[4-(4-Bromophenyl)piperazin-1-yl]-2-oxoethoxy}phenyl)-1,3-dimethyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

6-{4-[2-(4-Hydroxy-4-phenylpiperidin-1-yl)-2-oxoethoxy]phenyl}-1,3-dimethyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

1-{2-[4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy]acetyl}-4-phenylpiperidine-4-carbonitrile

6-{4-[2-(4,4-Diphenylpiperidin-1-yl)-2-oxoethoxy]phenyl}-1,3-dimethyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

6-(4-{2-[4-(4-Chlorophenyl)-4-hydroxypiperidin-1-yl]-2-oxoethoxy}phenyl)-1,3-dimethyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

6-(4-{2-[4-(3,5-Dichloropyridin-4-yl)piperazin-1-yl]-2-oxoethoxy}phenyl)-1,3-dimethyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

6-(4-{2-[4-(5-Chlorobenzothiazol-2-yl)piperazin-1-yl]-2-oxoethoxy}phenyl)-1,3-dimethyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

1,3-Dimethyl-6-{4-[2-oxo-2-(1,3,4,9-tetrahydro-b-carbolin-2-yl)ethoxy]phenyl}-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

6-[4-(2-{4-[1-(4-Fluorophenyl)methanoyl]piperidin-1-yl}-2-oxo-ethoxy)phenyl]-1,3-dimethyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

2-[4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)-phenoxy]-N-pyridin-4-ylmethylacetamide

4-{2-[4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy]ethanoyl}piperazine-1-carboxylic acid ethyl ester

6-(4-{2-[4-(2-Methoxyphenyl)piperidin-1-yl]-2-oxoethoxy}phenyl)-1-methyl-3-propyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

6-(4-{2-[4-(3,5-Dichloropyridin-4-yl)piperazin-1-yl]-2-oxoethoxy}phenyl)-1-methyl-3-propyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

N-(6-Methoxypyridin-3-yl)-2-[4-(1-methyl-2,4-dioxo-3-propyl-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy]acetamide

1-Methyl-6-(4-{2-oxo-2-[4-(4-trifluoromethylphenyl)piperazin-1-yl]ethoxy}phenyl)-3-propyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

6-[4-(2-Morpholin-4-yl-2-oxoethoxy)phenyl]-3-propyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

6-{4-[2-(4-Methylpiperazin-1-yl)-2-oxoethoxy]phenyl}-3-propyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

2-[4-(2,4-Dioxo-3-propyl-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy]-N-(2-hydroxyethyl)acetamide

6-(4-{2-[4-(2-Methoxyphenyl)piperazin-1-yl]-2-oxoethoxy}phenyl)-3-propyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

6-{4-[2-(4-Benzylpiperazin-1-yl)-2-oxoethoxy]phenyl}-3-propyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

2-[4-(2,4-Dioxo-3-propyl-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)-phenoxy]-N-(4-fluorophenyl)acetamide

N-(4-Bromophenyl)-2-[4-(2,4-dioxo-3-propyl-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy]acetamide

6-{4-[2-Oxo-2-(4-phenylpiperazin-1-yl)-ethoxy]phenyl}-1-propyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

6-(4-{2-[4-(4-Fluorophenyl)piperazin-1-yl]-2-oxo-ethoxy}phenyl)-3-methyl-1-(3-morpholin-4-ylpropyl)-1,5-dihydro-pyrrolo[3,2-d]pyrimidine-2,4-dione

3-Methyl-1-(3-morpholin-4-yl-propyl)-6-{4-[2-oxo-2-(4-phenyl-piperazin-1-yl)ethoxy]phenyl}-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

3-Methyl-1-(3-morpholin-4-yl-propyl)-6-(4-{2-oxo-2-[4-(4-trifluoromethyl-phenyl)-piperazin-1-yl]-ethoxy}phenyl)-1,5-dihydro-pyrrolo[3,2-d]pyrimidine-2,4-dione

Pyrazin-2-yl-carbamic acid 4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)benzyl ester

(2,6-Dimethoxy-pyrimidin-4-yl)-carbamic acid 4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)benzyl ester

Pyridin-4-ylmethyl carbamic acid 4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)benzyl ester

4-(3-Chlorophenyl)piperazine-1-carboxylic acid 4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)benzyl ester

(1H-Pyrazol-3-yl)carbamic acid 4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)benzyl ester

4-(3-Trifluoromethylphenyl)piperazine-1-carboxylic acid 4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)benzyl ester

Isoxazol-3-yl-carbamic acid 4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)benzyl ester

(4-Fluorophenyl)-carbamic acid 4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)benzyl ester

Benzylcarbamic acid 4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)benzyl ester

Phenylcarbamic acid 4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)benzyl ester

Pyridin-2-yl-carbamic acid 4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)benzyl ester

(5-Methylpyridin-2-yl)-carbamic acid 4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)-benzyl ester

Thiophen-2-yl-carbamic acid 4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)-benzyl ester

Thiophen-3-yl-carbamic acid 4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)-benzyl ester

Furan-2-yl-carbamic acid 4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)-benzyl ester

4-Phenylpiperazine-1-carboxylic acid 4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)-benzyl ester

3,4-Dihydro-1H-isoquinoline-2-carboxylic acid 4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)benzyl ester

Thiophen-2-yl-carbamic acid 2-[4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy]ethyl ester

(4-Bromophenyl)carbamic acid 2-[4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy]ethyl ester

1-[1-(2,6-Difluoro-phenyl)methanoyl]-3-[4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)benzyl]urea

6-[4-(5-Fluorobenzooxazol-2-ylmethoxy)phenyl]-1,3-dipropyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

6-[4-(1H-Benzoimidazol-2-ylmethoxy)phenyl]-1,3-dipropyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

1,3-Dimethyl-6-[4-(quinolin-2-ylmethoxy)phenyl]-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

1,3-Dimethyl-6-[4-(3-phenyl[1,2,4]oxadiazol-5-ylmethoxy)phenyl]-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

1-Methyl-6-[4-(3-phenyl[1,2,4]oxadiazol-5-ylmethoxy)phenyl]-3-propyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

6-{4-[3-(4-Fluorophenyl)[1,2,4]oxadiazol-5-ylmethoxy]phenyl}-1-methyl-3-propyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

6-[4-(5-Chlorobenzooxazol-2-ylmethoxy)phenyl]-1-methyl-3-propyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

6-{4-[3-(4-Bromophenyl)-[1,2,4]oxadiazol-5-ylmethoxy]-phenyl}-3-propyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

1,3-Dimethyl-6-{4-[1-(3-phenyl[1,2,4]oxadiazol-5-yl)ethoxy]phenyl}-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

6-(4-{1-[3-(4-Fluorophenyl)[1,2,4]oxadiazol-5-yl]ethoxy}phenyl)-1,3-dimethyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

1,3-Dimethyl-6-{4-[1-(3-thiophen-3-yl[1,2,4]oxadiazol-5-yl)ethoxy]phenyl}-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

1,3-Dimethyl-6-(4-{1-[3-(4-methylsulfanylphenyl)[1,2,4]oxadiazol-5-yl]ethoxy}phenyl)-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

6-{4-[(4-Bromophenylamino)methyl]phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

6-(4-Phenylaminomethylphenyl)-1,3-dipropyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

and pharmaceutically acceptable salts thereof.

Of outstanding interest are 6-phenylpyrrolopyrimidinedione derivatives of formula (I), and pharmaceutically acceptable salts thereof, wherein:

- R^1 and R^2 are the same or different and each independently represent a C_1-C_4 alkyl group;
- R^3 represents hydrogen or halogen;
- R^4 and R^5 are the same or different and each independently represent hydrogen, C_1-C_4 alkyl, C_1-C_4 alkoxy or C_1-C_4 alkylthio;
- L_1 is -O-CH_2-, -CH_2-O- or -CH_2NH-, for example –O-CH_2-; and

R^6 represents a phenyl group; an oxadiazolyl group which is unsubstituted or substituted by a phenyl group; or a group of formula $-C(O)NR^{10}R^{11}$, wherein either R^{10} is hydrogen and R^{11} is a thienyl group, a thiadiazolyl group, a pyridyl group, an optionally substituted phenylcarbonyl group or a phenyl group which is unsubstituted or substituted by 1 or 2 substituents selected from halogen atoms and phenyl and benzyloxy groups or R^{10} and R^{11} form, together with the N atom to which they are attached, a 1, 2, 3, 4-tetrahydroisoquinoline group, a 1,3,4,9-tetrahydro-beta-carbolinyl group, a piperidinyl group or a piperazinyl group, the piperidinyl and piperazinyl groups being unsubstituted or substituted by 1 or 2 groups selected from hydroxy, optionally substituted phenyl and optionally substituted pyridyl.

In this embodiment, R^6 may represent, for example, $-C(O)NR^{10}R^{11}$ or an oxadiazolyl group which is unsubstituted or substituted by a phenyl group, wherein either R^{10} is hydrogen and R^{11} is a thiadiazolyl group, a pyridyl group or a phenyl group which is unsubstituted or substituted by 1 or 2 substituents selected from halogen atoms and phenyl and benzyloxy groups or R^{10} and R^{11} form, together with the N atom to which they are attached, a 1, 2, 3, 4-tetrahydroisoquinoline group, a piperidinyl group or a piperazinyl group, the piperidinyl and piperazinyl groups being unsubstituted or substituted by 1 or 2 phenyl groups.

Examples of such compounds include:

6-{4-[2-Oxo-2-(4-phenylpiperazin-1-yl)ethoxy]phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

6-{4-[2-(3,4-Dihydro-1*H*-isoquinolin-2-yl)-2-oxoethoxy] phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

2-[4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(4-fluorophenyl) acetamide

1,3-Dimethyl-6-{4-[2-oxo-2-(4-phenylpiperazin-1-yl)ethoxy]phenyl}-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

N-Biphenyl-4-yl-2-[4-(1-methyl-2,4-dioxo-3-propyl-2,3,4,5-tetrahydro-1*H*-

pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] acetamide

6-{4-[2-(4,4-Diphenylpiperidin-1-yl)-2-oxo-ethoxy] phenyl}-1-methyl-3-propyl-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione

6-[4-(3-Phenyl-[1,2,4]oxadiazol-5-ylmethoxy)phenyl]-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

N-(4-Bromophenyl)-2-[4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-3-methoxyphenoxy]acetamide

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(4-fluorophenyl) acetamide

2-[4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-[1,3,4]thiadiazol-2-ylacetamide

2-[4-(7-Bromo-2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(4-fluorophenyl)acetamide

N-(4-Benzyloxyphenyl)-2-[4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] acetamide

2-[4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-2-methoxyphenoxy]-*N*-(4-fluorophenyl)acetamide

Thiophen-3-yl-carbamic acid 4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)benzyl ester

6-(4-{2-[4-(4-Chlorophenyl)-4-hydroxypiperidin-1-yl]-2-oxoethoxy}phenyl)-1,3-dimethyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

6-(4-{2-[4-(3,5-Dichloropyridin-4-yl)piperazin-1-yl]-2-oxoethoxy}phenyl)-1-methyl-3-propyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

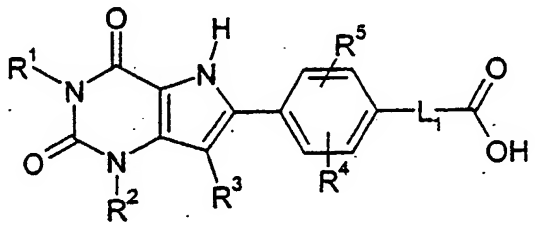
1,3-Dimethyl-6-{4-[2-oxo-2-(1,3,4,9-tetrahydro-b-carbolin-2-yl)ethoxy]phenyl}-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

1-[1-(2,6-Difluorophenyl)methanoyl]-3-[4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)benzyl]urea

6-(4-Phenylaminomethylphenyl)-1,3-dipropyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

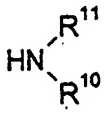
and pharmaceutically acceptable salts thereof.

According to a further feature of the present invention, the 6-phenyl-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione derivatives of general formula (I) in which R^6 is $-CONR^{10}R^{11}$ can be prepared by reaction of the corresponding carboxylic acids of formula (II):



(II)

(wherein R^1, R^2, R^3, R^4, R^5, and L_1 are as hereinbefore defined) and the corresponding amines (III):

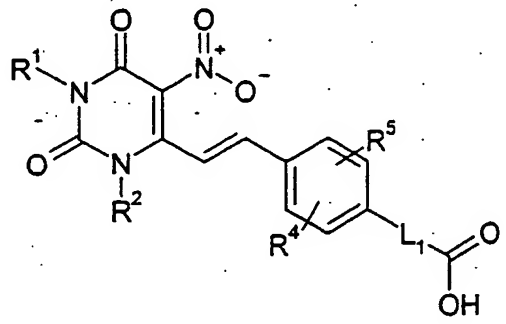


(III)

(wherein R^{10} and R^{11} are as hereinbefore defined). The reaction is carried out in an organic solvent, preferably a polar aprotic organic solvent such as dichloromethane, *N,N*-dimethylformamide or tetrahydrofuran, at a temperature from 10°C to 60°C and in the presence of an organic base, preferably an amine base such as triethylamine or polymer supported morpholine, and in the presence of standard coupling agents such as 1-hydroxybenzotriazole and 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride.

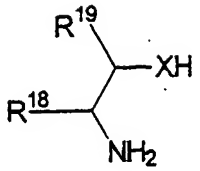
The thus obtained compound of formula (I) can be converted to a further compound of formula (I) by standard functional group interconversions known to those of skill in the art. Thus, for example, in the case that R^3 is chlorine or bromine, the carboxylic acid of formula (II) is obtained from the compound of formula (II) where R^3 is hydrogen by chlorination or bromination using methods known *per se*.

The 6-phenylpyrrolopyrimidinedione derivatives of general formula (I) are also prepared from vinyl derivatives (IV) (wherein R^1, R^2, R^4, R^5, and L_1 are as hereinbefore defined) and amines (III) using the coupling procedure described below and subsequent reductive cyclization mediated by triethyl phosphite or sodium dithionite in formic acid both at reflux temperature.

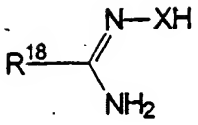


(IV)

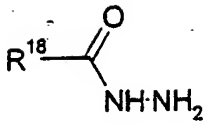
When R^6 is a said group of formula (H), wherein X, Y^1 and Y^2 are as hereinbefore defined, the ring of R^6 is prepared from carboxylic acid (II) and amines (V) or amide derivatives (VI) by amide type coupling followed by cyclodehydration typically performed in toluene with catalytic amounts of acid or in dichloromethane or tetrahydrofuran using dehydration agents (such as $SOCl_2$, $POCl_3$, Burgess reagent or polyphosphoric acid) and in the products derived from amine (V) a further oxidation can be done, typically performed by NiO_2 or MnO_2.



(V)



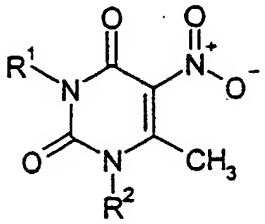
(VI)



(VII)

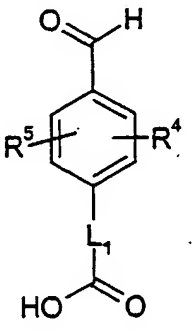
The 6-phenylpyrrolopyrimidinedione derivatives of general formula (II) are prepared from vinyl derivatives (IV) by reductive cyclization using the methods described hereinbefore.

The vinyl derivatives of general formula (IV) are prepared by reaction of the corresponding 6-methyl-5-nitrouracils (VIII):



(VIII)

(wherein R^1 and R^2 are as hereinbefore defined), and the corresponding benzaldehydes (IX):

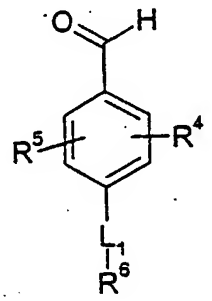


(IX)

(wherein L_1, R^4 and R^5 are as hereinbefore defined) by methods known *per se*, e.g. C. E. Müller et al., *J. Med. Chem.* **1994**, *37*, 1526-1534 and references cited therein.

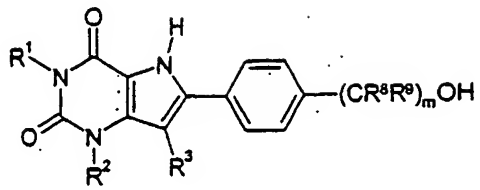
When R^6 is $-ON=CR^{12}R^{13}$, the products of general formula (I) are prepared by reacting a carboxylic acid of formula (II) with a compound of formula R^{12}-$C(R^{13})$=N-OH using standard coupling procedures known in the art.

When R^6 is $-S(O)_2-NR^{10}R^{11}$, aryl, heterocyclyl or heteroaryl the products of general formula (I) are prepared by condensation of the 6-methyl-5-nitrouracils (VIII) with the corresponding benzaldehydes (X) to give the vinyl derivatives, followed by reductive cyclization as in the preparation of compounds of general formula (II).

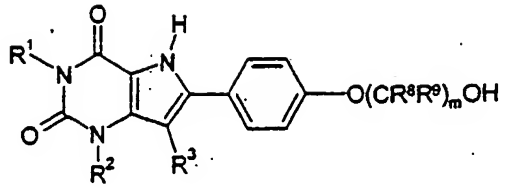


(X)

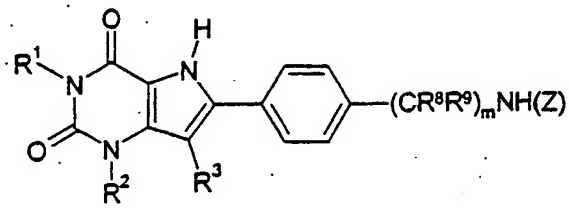
When L_1 is $-(CR^8R^9)_mO-$, $-O(CR^8R^9)_mO$ or $-(CR^8R^9)_mN(Z)-$ the products of general formula (I) are prepared by condensation of the alcohols (XI), (XII) or amine (XIII) with the corresponding isocianates to give the carbamate or urea derivatives.



(XI)



(XII)



(XIII)

Compounds (XI) and (XII) are prepared by reduction of the carboxylic acid of general formula (II) wherein L_1 is $-(CR^8R^9)_{m-1}-$ or $-O(CR^8R^9)_{m-1}-$ using standard reductive agents such as borane or aluminium hydrides in common organic solvents such as tetrahydrofuran at a temperature from 0°C to 100°C.

Compounds of general formula (XIII) can be obtained from alcohols (XI) by using standard procedures known in the art.

The 6-methyl-5-nitrouracils (VIII) can be prepared from the corresponding *N,N'*-disubstituted ureas by methods known *per se*, e.g. S. Senda et al., *J. Med. Chem.* **1972**, *15*, 471-476 or H. Egg *Synthesis* **1982**, 1071-1072 and references cited therein. The compounds of formulae (III), (V), (VI), (VII), (VIII), (IX) and (X) are known compounds or may be prepared by analogy with known methods. The compounds of formula R^{12}-C(R^{13})=N-OH are commercially available or may be prepared by analogy with known methods.

The 6-phenyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione derivatives of formula (I) in which there is the presence of a basic group can be converted by methods known *per se* into pharmaceutically acceptable salts, preferably acid addition salts by

treatment with organic or inorganic acids such as fumaric, tartaric, succinic or hydrochloric acid. Also 6-phenyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione derivatives of formula (I) in which there is the presence of an acidic group, may be converted into pharmacologically acceptable salts by reaction with an alkali metal hydroxide such as sodium or potassium hydroxide or an organic base such as diethanolamine. The acid or alkali addition salts so formed may be interchanged with suitable pharmaceutically acceptable counter ions using processes known *per se*.

Adenosine 2b receptor subtype competition radioligand binding

Human membranes from recombinant A2b receptors were purchased from Receptor Biology, Inc.(USA).

Competition assays were carried out by incubation of membranes from hA2b receptors transfected to HEK293 cells, [^{3}H]DPCPX as radioligand, buffer (50mM Tris-HCl (pH 6.5), 10mM $MgCl_2$, 1mM EDTA, 0.1mM benzamidine, 2units/ml adenosine deaminase), and unlabelled ligand in a total volume of 0.1 ml for 30 min at 25°C. NECA was used to determinate non-specific binding. Filter over Schleicher&Schuell GF/52 filters (pre-soaked 0.5% polyethylenyimine) in a Brandel cell harvester. Unbound radioligand was removed with 4x2 ml ice-cold 50 mM Tris-Hcl 50 mM (pH 6.5).

Adenosine 2a receptor subtype competition radioligand binding

Human membranes from recombinant A2a receptors were purchased from Receptor Biology, Inc.(USA).

Competition assays were carried out by incubation of membranes from hA2a receptors transfected to HEK293 cells, [^{3}H]ZM241385 as radioligand, buffer (50mM Tris-HCl (pH 7.4), 10mM $MgCl_2$, 1mM EDTA, 2units/ml adenosine deaminase), and unlabelled ligand in a total volume of 0.2 ml for 90 min at 25°C. NECA was used to determinate non-specific binding. Filter over Schleicher&Schuell GF/52 filters (pre-soaked 0.5% polyethylenyimine) in a Brandel cell harvester. Unbound radioligand was removed with 3x3 ml ice-cold 50 mM Tris-Hcl 50 mM (pH 7.4), 0.9% NaCl.

The results are shown in Table 1 and Table 2.

TABLE 1

Example	IC_{50} A2b (nM)
2	7
4	3
58	5
68	8
99	9
100	10
210	17
156	6
3	5
67	24

It can be seen from Table 1 that the compounds of formula (I) are potent inhibitors of the A2b adenosine receptor subtype. Preferred 6-phenyl-1,5-dihydropyrrolo [3,2-*d*]pyrimidine-2,4-dione derivatives of the invention possess an IC_{50} value for the inhibition of A2b (determined as defined above) of less than 50 nM, preferably less than 10 nM and most preferably less than 5 nM.

TABLE 2

Example	IC_{50} A2a (nM)
3	22
67	26
138	38
26	42
160	84

It can be seen from Table 2 that the compounds of formula (I) are potent inhibitors of the A2a adenosine receptor subtype. Some preferred 6-phenyl-1,5-dihydro pyrrolo[3,2-*d*]pyrimidine-2,4-dione derivatives of the invention possess an IC_{50} value for the inhibition of A2a (determined as defined above) of less than 100 nM, preferably less than 50 nM and most preferably less than 10 nM.

The 6-phenyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione derivatives of the invention are useful in the treatment or prevention of asthma, bronchoconstriction, allergic potentiation, inflamation or reperfusion injury, myocardial ischemia, inflammation, diarrheal diseases, brain arteriole diameter constriction, Parkinson's disease, non insulin dependent diabetes mellitus, release of allergic mediators, and/or treatment of an autoimmune diseases. Examples of autoimmune diseases which can be treated or prevented using the compounds of the invention are Addison's disease, autoimmune hemolytic anemia, Crohn's disease, Goodpasture's syndrome, Grave's disease, Hashimoto's thyroiditis, idiopathic thrombocytopinic purpura, insulin-dependent diabetes mellitus, multiple sclerosis, myasthenia gravis, pemphigus vulgaris, pernicious anemia, poststreptococcal glomerulonephritis, psoriasis, rheumatoid arthritis, scleroderma, Sjogren's syndrome, spontaneous infertility, and syntemic lupus erythematosus.

Accordingly, the 6-phenyl-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione derivatives of the invention and pharmaceutically acceptable salts thereof, and pharmaceutical compositions comprising such compound and/or salts thereof, may be used in a method of treatment of disorders of the human body which comprises administering to a patient requiring such treatment an effective amount of a 6-phenyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione derivative of the invention or a pharmaceutically acceptable salt thereof.

The present invention also provides pharmaceutical compositions which comprise, as an active ingredient, at least a 6-phenyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione derivative of formula (I) or a pharmaceutically acceptable salt

thereof in association with a pharmaceutically acceptable excipient such as a carrier or diluent. The active ingredient may comprise 0.001% to 99% by weight, preferably 0.01% to 90% by weight of the composition depending upon the nature of the formulation and whether further dilution is to be made prior to application. Preferably the compositions are made up in a form suitable for oral, topical, nasal, rectal, percutaneous or injectable administration.

The pharmaceutically acceptable excipients which are admixed with the active compound, or salts of such compound, to form the compositions of this invention are well-known *per se* and the actual excipients used depend *inter alia* on the intended method of administering the compositions.

Compositions of this invention are preferably adapted for injectable and *per os* administration. In this case, the compositions for oral administration may take the form of tablets, retard tablets, sublingual tablets, capsules, inhalation aerosols, inhalation solutions, dry powder inhalation, or liquid preparations, such as mixtures, elixirs, syrups or suspensions, all containing the compound of the invention; such preparations may be made by methods well-known in the art.

The diluents which may be used in the preparation of the compositions include those liquid and solid diluents which are compatible with the active ingredient, together with colouring or flavouring agents, if desired. Tablets or capsules may conveniently contain between 2 and 500 mg of active ingredient or the equivalent amount of a salt thereof.

The liquid composition adapted for oral use may be in the form of solutions or suspensions. The solutions may be aqueous solutions of a soluble salt or other derivative of the active compound in association with, for example, sucrose to form a syrup. The suspensions may comprise an insoluble active compound of the invention or a pharmaceutically acceptable salt thereof in association with water, together with a suspending agent or flavouring agent.

Compositions for parenteral injection may be prepared from soluble salts, which may or may not be freeze-dried and which may be dissolved in pyrogen free aqueous media or other appropriate parenteral injection fluid.

Effective doses are normally in the range of 2-2000 mg of active ingredient per day. Daily dosage may be administered in one or more treatments, preferably from 1 to 4 treatments, per day.

The syntheses of the compounds of the invention and of the intermediates for use therein are illustrated by the following Examples (including Preparation Examples (Preparations 1-26)) which do not limit the scope of the invention in any way.

^{1}H Nuclear Magnetic Resonance Spectra were recorded on a Varian Gemini 300 spectrometer. Melting points were recorded using a Perkin Elmer DSC-7 apparatus. The chromatographic separations were obtained using a Waters 2690 system equipped with a Symmetry C18 (2.1 x 10 mm, 3.5 μM) column. As detectors a Micromass ZMD mass spectrometer using ES ionization and a Waters 996 Diode Array detector were used. The mobile phase was formic acid (0.46 mL), ammonia (0.115 mL) and water (1000 mL) (A) and formic acid (0.4 mL), ammonia (0.1 mL), methanol (500 mL) and acetonitrile (500 mL) (B): initially from 0% to 95% of B in 20 min, and then 4 min. with 95% of B. The reequilibration time between two injections was 5 min. The flow rate was 0.4 mL/min. The injection volume was 5 μL. Diode array chromatograms were processed at 210 nm.

PREPARATION EXAMPLES

PREPARATION 1

{4-[2-(5-Nitro-2,6-dioxo-1,3-dipropyl-1,2,3,6-tetrahydropyrimidin-4-yl)vinyl]phenoxy}acetic acid

To a solution of 6-methyl-5-nitro-1,3-dipropyl-1*H*-pyrimidine-2,4-dione (4.1 g, 16.08 mmol) in dry dioxane (52 mL) was added piperidine (1.6 mL, 18.35 mmol) and (4-formylphenoxy)acetic acid (2.9 g, 16.08 mmol). The mixture was stirred at reflux

temperature for 68 hours. The resulting solution was concentrated under vacuum and the residue was treated with ethanol (100 mL) until formation of a precipitate was observed. The solid was collected by filtration and dried under vacuum to yield the title product (4.8 g, 72%) as a yellow solid.

m.p.(H_2O): 72-74 °C.

δ ^{1}H NMR (DMSO): 10.10 (bs, 1H), 7.61 (d, 2H), 6.99 (m, 4H), 4.76 (s, 2H), 3.84 (m, 4H), 1.61 (m, 4H), 0.87 (m, 6H).

ESI/MS (m/e, %): 418 [$(M+1)^+$, 100].

PREPARATION 2

[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]acetic acid

a)A solution of 6-methyl-5-nitro-1,3-dipropyl-1*H* pyrimidine-2,4-dione (7.72 g, 30.24 mmol), (4-formylphenoxy)acetic acid (6 g, 33.26 mmol) and piperidine (4.5 mL, 45.36 mmol) in ethanol (140 mL) with 3A molecular sieves (9.8 g) was refluxed for 5 hours. The resulting suspension was diluted with dichloromethane (75 mL), filtrated and the filtrates were evaporated under reduced pressure. The residue was suspended in water (100 mL) and acetic acid was added until pH was slightly acidic. The aqueous suspension was partitioned between dichloromethane and brine, then the organic phase was separated, washed with 2N HCl, brine, dried ($MgSO_4$) and evaporated under reduced pressure. The residue was triturated with a mixture of ethyl ether and isopropyl ether. The precipitate was collected by filtration and dried under vacuum to yield the compound of Preparation 1 (8.08 g, 64%).

b)To a stirred solution of the above compound (8.08 g, 19.36 mmol) in formic acid (180 mL) was slowly added sodium dithionite (19.8 g, 96.8 mmol) and the mixture was refluxed overnight. The resulting solution was cooled to room temperature and poured into water (750 mL). The precipitate was collected by filtration and washed with water and ethyl ether, then dried under vacuum to yield [4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]acetic acid (5.6 g, 75%) as

a white solid.

m.p.(MeOH/H_2O): 280-282 °C.

δ ^{1}H NMR (DMSO): 7.85 (d, 2H), 6.98 (d, 2H), 6.64 (d, 1H), 4.74 (s, 2H), 3.87 (m, 4H), 1.62 (m, 4H), 0.90 (m, 6H).

ESI/MS (m/e, %): 386 [$(M+1)^+$, 100].

PREPARATION 3

[4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]acetic acid ethyl ester

a)Following the same procedure as in Preparation 1, from 1,3,6-trimethyl-5-nitro-1*H*-pyrimidine-2,4-dione (2.47 g, 12.4 mmol) and (4-formylphenoxy)acetic acid ethyl ester (2.58 g, 12.4 mmol), {4-[2-(1,3-Dimethyl-5-nitro-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-yl)vinyl]phenoxy}acetic acid ethyl ester was obtained (2.4 g, 50%) as a yellow solid.

m.p.(EtOH): 136-138 °C.

δ ^{1}H NMR ($CDCl_3$):7.43 (d, 2H), 7.00 (d, 1H), 6.92 (d, 2H), 6.52 (d, 1H), 4.66 (s, 2H), 4.28 (q, 2H), 3.48 (s, 3H), 3.41 (s, 3H), 1.30 (t, 3H).

b)A solution of the above ester (1.18 g, 3.025 mmol) in triethyl phosphite (5 mL) was refluxed for 7 hours. The resulting mixture was cooled, the precipitate collected by filtration and washed with ethyl ether to yield [4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*] pyrimidin-6-yl)phenoxy]acetic acid ethyl ester (0.32 g, 30%) as a white solid.

m.p.(MeOH/H_2O): 243-245 °C.

δ ^{1}H NMR (DMSO): 12.45 (bs, 1H), 7.95 (d, 2H), 7.10 (d, 2H), 6.72 (s, 1H), 4.94 (s, 2H), 4.28 (q, 2H), 3.52 (s, 3H), 3.36 (s, 3H), 1.32 (t, 3H).

ESI/MS (m/e, %): 357 (M^+, 80), 270 (100).

PREPARATION 4

[4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]acetic acid

Obtained as a white solid (44% overall) from 1,3,6-trimethyl-5-nitro-1*H*-pyrimidine-2,4-dione and (4-formylphenoxy)acetic acid following the procedure described in Preparation 2.

m.p.(MeOH/H_2O): 261-263 °C.

δ ^{1}H NMR (DMSO): 12.89 (bs, 1H), 12.19 (s, 1H), 7.76 (d, 2H), 6.89 (d, 2H), 6.54 (d, 1H), 4.65 (s, 2H), 3.33 (s, 3H), 3.17 (s, 3H).

ESI/MS (m/e, %): 329 (M^+, 5).

PREPARATION 5

[4-(1,3-Diethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]acetic acid

Obtained as a white solid (41% overall) from 1,3-diethyl-6-methyl-5-nitro-1*H*-pyrimidine-2,4-dione and (4-formylphenoxy)acetic acid following the procedure described in Preparation 2.

δ ^{1}H NMR (DMSO): 12.38 (bs, 1H), 7.82 (d, 2H), 7.01 (d, 2H), 6.62 (s, 1H), 4.78 (s, 2H), 3.98 (m, 4H), 1.20 (m, 6H).

PREPARATION 6

[4-(1-Methyl-2,4-dioxo-3-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]acetic acid

Obtained as a white solid (60% overall) from 1,6-dimethyl-5-nitro-3-propyl-1*H*-pyrimidine-2,4-dione and (4-formylphenoxy)acetic acid following the procedure described in Preparation 2.

m.p.: 300-301 °C.

δ ^{1}H NMR (DMSO): 13.5 (bs, 1H), 12.2 (bs, 1H), 7.9 (d, 2H), 7.1 (d, 2H), 6.8 (s, 2H), 4.8 (s, 2H), 3.9 (t, 2H), 3.4 (s, 3H), 1.6 (m, 2H), 0.9 (t, 3H).

ESI/MS (m/e, %): 357 [$(M+1)^+$, 91].

PREPARATION 7

[4-(3-Methyl-2,4-dioxo-1-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-phenoxy]acetic acid

Obtained as a yellow solid (48% overall) from 3,6-dimethyl-5-nitro-1-propyl-1*H*-pyrimidine-2,4-dione and (4-formylphenoxy)acetic acid following the procedure described in Preparation 2.

δ ^{1}H NMR (DMSO): 13.0 (bs, 1H), 12.2 (bs, 1H), 7.9 (d, 2H), 7.0 (d, 2H), 6.7 (s, 2H), 4.7 (s, 2H), 3.9 (t, 2H), 3.3 (s, 3H), 1.7 (m, 2H), 0.9 (t, 3H).

PREPARATION 8

{4-[1-(3-Methoxypropyl)-3-methyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl]phenoxy}acetic acid ethyl ester

Obtained as white solid (17% overall) from 1-(3-methoxypropyl)-3,6-dimethyl-5-nitro-1*H*-pyrimidine-2,4-dione and (4-formylphenoxy)acetic acid ethyl ester following the procedure described in Preparation 3.

m.p.(MeOH/H_2O): 177-179 °C.

δ ^{1}H NMR ($CDCl_3$): 11.7 (s, 1H), 7.85 (d, 2H), 6.95 (d, 2H), 6.46 (d, 1H), 4.67 (s, 2H), 4.30 (q, 2H), 4.07 (t, 2H), 3.48 (s, 3H), 3.43 (m, 2H), 3.34 (s, 3H), 2.05 (m, 2H), 1.32 (t, 3H).

ESI/MS (m/e, %): 415 (M^+, 65).

PREPARATION 9

[4-(3-Isobutyl-1-methyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]acetic acid

Obtained as a white solid (50% overall) from 3-isobutyl-1,6-dimethyl-5-nitro-1*H*-pyrimidine-2,4-dione and (4-formylphenoxy)acetic acid following the procedure described in Preparation 2.

δ ^{1}H NMR (DMSO): 13.00 (bs, 1H), 12.45 (bs, 1H), 7.95 (m, 2H), 6.90 (m, 2H), 6.72 (s, 1H), 4.74 (s, 2H), 3.72 (d, 2H), 3.26 (s, 3H), 2.10 (m, 1H), 0.90 (d, 6H).

PREPARATION 10

[4-(2,4-Dioxo-1-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]acetic acid

Obtained as a yellow solid (45% overall) from 6-methyl -5-nitro-1-propyl-1*H*-pyrimidine-2,4-dione and (4-formylphenoxy)acetic acid following the procedure described in Preparation 2.

m.p.: 306-307 °C.

δ ^{1}H NMR (DMSO): 11.99 (bs, 1H), 10.57 (s, 1H), 7.62 (d, 2H), 6.75 (d, 2H), 6.40 (s, 1H), 4.51 (s, 2H), 3.57 (t, 2H), 1.44 (m, 2H), 0.68 (t, 3H).

PREPARATION 11

{4-[1,3-Bis(2-methoxyethyl)-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl]phenoxy}acetic acid

Obtained as a white solid (30% overall) from 5-amino-1,3-bis(2-methoxyethyl)-6-methyl-1*H*-pyrimidine-2,4-dione and (4-formylphenoxy)acetic acid following the procedure described in Preparation 2.

δ ^{1}H NMR (DMSO): 13.10 (bs, 1H), 12.25 (bs, 1H), 7.82 (d, 2H), 7.05 (d, 2H), 6.63 (s, 1H), 4.78 (s, 2H), 4.05 (m, 4H), 3.58 (m, 4H), 3.38 (s, 3H), 3.24 (s, 3H).

PREPARATION 12

{4-[1,3-Bis(cyclopropylmethyl)-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl]phenoxy}acetic acid

Obtained as a white solid (45% overall) from 5-amino-1,3-bis(cyclopropylmethyl)-6-methyl-1*H*-pyrimidine-2,4-dione and (4-formylphenoxy)acetic acid following the procedure described in Preparation 2.

δ ^{1}H NMR (DMSO): 13.10 (bs, 1H), 12.28 (bs, 1H), 7.88 (d, 2H), 7.02 (d, 2H),

6.72 (s, 1H), 4.76 (s, 2H), 3.81 (m, 4H), 1.25 (m, 2H), 0.38 (m, 8H).

PREPARATION 13

[4-(7-Chloro-1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]acetic acid

To a solution of the title compound of Preparation 4 (0.5 g, 1.52 mmol) in glacial acetic acid (3 mL) was slowly added sulfuryl chloride (0.13 mL) and the mixture was stirred at room temperature for 4 hours. The reaction mixture was carefully poured into stirred ice-water and the aqueous suspension was partitioned between dichloromethane and brine, then the organic phase was separated, washed with water, dried ($MgSO_4$) and evaporated under reduced pressure to yield the title product (500 mg, 90%) as an off white solid.

δ ^{1}H NMR (DMSO): 12.7 (s, 1H), 7.6 (d, 2H), 7.0 (d, 2H), 4.8 (s, 2H), 3.7 (s, 3H), 3.3 (s, 3H).

PREPARATION 14

[4-(7-Bromo-2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]acetic acid

To a solution of the title compound of Preparation 2 (1 g, 2.59 mmol) in glacial acetic acid (22 mL) was slowly added bromine (0.187 mL, 3.63 mmol) and the mixture was stirred at room temperature for 1 hour. Then the reaction mixture was poured into ice-water and partitioned between dichloromethane and brine, the organic phase was separated, dried ($MgSO_4$) and evaporated under reduced pressure to yield the title product (0.88 g, 73%) as an orange solid.

δ ^{1}H NMR (DMSO): 12.7 (s, 1H), 7.5 (d, 2H), 6.9 (d, 2H), 4.7 (s, 2H), 4.1 (t, 2H), 3.8 (t, 2H), 1.5 (m, 4H), 0.86 (dt, 6H).

PREPARATION 15

[4-(7-Chloro-2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]acetic acid

Obtained as a yellow solid (89%) from the title compound of Preparation 2 following the procedure described in Preparation 13.

δ ^{1}H NMR (DMSO): 12.7 (s, 1H), 7.6 (d, 2H), 7.0 (d, 2H), 4.7 (s, 2H), 4.1 (t, 2H), 3.9 (t, 2H), 1.6 (m, 4H), 0.9 (dt, 6H).

PREPARATION 16

[4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo [3,2-*d*]pyrimidin-6-yl)-3-methoxyphenoxy]acetic acid

a)Following the same procedure as in Preparation 3, from 1,3,6-trimethyl-5-nitro-1*H*-pyrimidine-2,4-dione and (4-formyl-3-methoxyphenoxy)acetic acid ethyl ester, [4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)-3-methoxyphenoxy]acetic acid ethyl ester was obtained (50% overall) as a yellow solid.

m.p.(EtOH/H_2O): 234-236 °C.

δ ^{1}H NMR (DMSO): 11.75 (bs, 1H), 7.66 (d, 1H), 6.65 (d, 1H), 6.54 (dd, 1H), 6.48 (s, 1H), 4.81 (s, 2H), 4.14 (q, 2H), 3.83 (s, 3H), 3.36 (s, 3H), 3.20 (s, 3H), 1.17 (t, 3H).

ESI/MS (m/e, %): 387 (M^+, 100).

b)A stirred mixture of the above compound (1.43 g, 3.7 mmol) and 10% NaOH (37 mL) in ethanol (37 mL) was heated to reflux temperature for 1 hour. The resulting mixture was concentrated under reduced pressure and the residue was treated with 10% HCl. The precipitate was collected by filtration and washed with EtOH to yield the title product (1.3 g, 99%) as a white solid.

m.p.(MeOH/H_2O): >260 °C (dec.).

δ ^{1}H NMR (DMSO): 11.84 (bs, 1H), 7.72 (d, 1H), 6.71 (s, 1H), 6.54 (m, 2H), 4.77 (s, 2H), 3.89 (s, 3H), 3.43 (s, 3H), 3.27 (s, 3H).

PREPARATION 17

[4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo [3,2-*d*]pyrimidin-6-yl)-2-methoxyphenoxy]acetic acid

Obtained as a white solid (25% overall) from 1,3,6-trimethyl-5-nitro-1*H*-pyrimidine-2,4-dione and (4-formyl-2-methoxyphenoxy)acetic acid ethyl ester following the procedure described in Preparation 16.

m.p.($MeOH/H_2O$): >300 °C (dec.).

δ ^1H NMR (DMSO): 12.3 (bs, 1H), 7.60 (s, 1H), 7.42 (d, 1H), 6.91 (d, 1H), 6.68 (s, 1H), 4.73 (s, 2H), 3.88 (s, 3H), 3.43 (s, 3H), 3.27 (s, 3H).

PREPARATION 18

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]propionic acid

Obtained as a yellow solid (41% overall) from 1,3-dipropyl-6-methyl-5-nitro-1*H*-pyrimidine-2,4-dione and 2-(4-formylphenoxy)propionic acid following the procedure described in Preparation 2.

δ ^1H NMR (DMSO): 11.5 (s, 1H), 7.5 (d, 2H), 7.0 (d, 2H), 6.1 (s, 1H), 4.9(q, 1H), 4.0 (t, 2H), 3.9 (t, 2H), 1.8 (d,3H), 1.7 (m, 4H), 0.9 (t, 6H).

PREPARATION 19

2-[4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]propionic acid

Obtained as a yellow solid (53% overall) from 1,3,6-trimethyl-5-nitro-1*H*-pyrimidine-2,4-dione and 2-(4-formylphenoxy)propionic acid following the procedure described in Preparation 2.

δ ^1H NMR (DMSO): 12.2 (s, 1H), 7.8 (d, 2H), 6.9 (d, 2H), 3.9 (m, 1H), 3.4 (s, 3H), 3.2 (s, 3H), 0.9 (dt, 3H).

PREPARATION 20

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]butyric acid

Obtained as white solid (65% overall) from 6-methyl-5-nitro-1,3-dipropyl-1*H* pyrimidine-2,4-dione and 2-(4-formylphenoxy)butyric acid following the procedure described in Preparation 2.

δ ^{1}H NMR ($CDCl_3$): 11.60 (bs, 1H), 7.51 (d, 2H), 7.02 (d, 2H), 4.78 (t, 1H), 4.05 (t, 2H), 3.94 (t, 2H), 2.18 (m, 2H), 1.77 (m, 4H), 1.22 (t, 3H), 0.98 (dt, 6H).

PREPARATION 21

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-2-methylpropionic acid

Obtained as white solid (25% overall) from 6-methyl-5-nitro-1,3-dipropyl-1*H* pyrimidine-2,4-dione and 2-(4-formylphenoxy)-2-methylpropionic acid following the procedure described in Preparation 2.

δ ^{1}H NMR ($CDCl_3$): 11.6 (s, 1H), 7.4 (d, 2H), 7.0 (d, 2H), 6.0 (s, 1H), 4.0 (t, 2H), 3.9 (t, 2H), 1.7 (m, 10H), 0.9 (t, 6H).

PREPARATION 22

[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]phenylacetic acid

Obtained as white solid (90% overall) from 6-methyl-5-nitro-1,3-dipropyl-1*H*-pyrimidine-2,4-dione and (4-formylphenoxy)phenylacetic acid following the procedure described in Preparation 2.

δ ^{1}H NMR ($CDCl_3$): 11.5 (s, 1H), 7.7 (d, 2H), 7.5 (d, 2H), 7.1 (d, 2H), 6.1 (s, 1H), 5.8 (s, 1H), 3.9 (m, 4H), 1.7 (m, 4H), 0.9 (dt, 6H).

PREPARATION 23

3-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenyl]propionic acid

Obtained as white solid (22% overall) from 6-methyl-5-nitro-1,3-dipropyl-1*H* pyrimidine-2,4-dione and 3-(4-formylphenyl)propionic acid following the procedure described in Preparation 2.

δ ^{1}H NMR ($CDCl_3$): 12.3 (s, 1H), 12.1 (s, 1H), 7.8 (2H, d), 7.3 (d, 2H), 6.7 (s, 1H), 3.8 (m, 4H), 2.8 (t, 2H), 2.5 (t, 2H), 1.6 (m, 4H), 0.9 (dt, 6H).

PREPARATION 24

3-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenyl]acrylic acid

Obtained as white solid (20% overall) from 6-methyl-5-nitro-1,3-dipropyl-1*H* pyrimidine-2,4-dione and 3-(4-formylphenyl)acrylic acid following the procedure described in Preparation 2.

δ ^{1}H NMR (DMSO): 12.3 (s, 1H), 7.9 (d, 2H), 7.7 (d, 2H), 7.5 (d, 1H), 6.8 (s, 1H), 6.5 (d, 1H), 3.8 (m, 4H), 1.5 (m, 4H), 0.8 (dt, 6H).

PREPARATION 25

4-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]butyric acid

Obtained as white solid (45% overall) from 6-methyl-5-nitro-1,3-dipropyl-1*H* pyrimidine-2,4-dione and 4-(4-formylphenoxy)butyric acid following the procedure described in Preparation 2.

δ ^{1}H NMR ($CDCl_3$): 11.7 (s, 1H), 7.7 (d, 2H), 6.9 (d, 2H), 6.1 (s, 1H), 4.2 (bs, 2H), 3.9 (m, 4H), 2.1 (bs, 2H), 1.7 (m, 4H), 0.9 (m, 6H).

PREPARATION 26

4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo [3,2-*d*]pyrimidin-6-yl)benzoic acid

Obtained as yellow solid (36% overall) from 6-methyl-5-nitro-1,3-dipropyl-1*H* pyrimidine-2,4-dione and 4-formylbenzoic acid following the procedure described in Preparation 2.

δ ^{1}H NMR (DMSO): 13.0 (bs, 1H), 12.6 (s, 1H), 8.0 (dd, 4H), 6.9 (s, 1H), 3.9 (m, 4H), 1.6 (m, 4H), 0.9 (dt, 6H).

PREPARATION 27

[4-(2,4-Dioxo-3-propyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]acetic acid

Obtained as a yellow solid (6% overall) from 6-methyl-5-nitro-3-propyl-1*H*-pyrimidine-2,4-dione and (4-formylphenoxy)acetic acid following the same procedure described in Preparation 2.

δ ^{1}H NMR (DMSO): 12.9 (s, 1H), 11.9 (s, 1H), 11.0 (s, 1H), 7.8 (d, 2H), 6.9 (d, 2H), 6.2 (d, 1H), 4.7 (s, 2H), 3.8 (t, 2H), 1.6 (m, 2H), 0.9 (t, 3H).

PREPARATION 28

{4-[3-Methyl-1-(3-morpholin-4-ylpropyl)-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl]phenoxy}acetic acid hydrochloride

a) A solution of 3,6-dimethyl-1-(3-morpholin-4-ylpropyl)-5-nitro-1*H*-pyrimidine-2,4-dione (0.50 g, 1.60 mmol), (4-formylphenoxy)acetic acid (0.31 g, 1.76 mmol) and piperidine (79 µL, 0.80 mmol) in ethanol (8 mL) with 3A molecular sieves (0.83 g) was refluxed for 3 hours. The resulting suspension was filtrated and the filtrates were evaporated under reduced pressure. The residue was suspended in water (100 mL), extracted with dichloromethane and water was evaporated under reduced pressure to yield (4-{-2-[1-methyl-3-(3-morpholin-4-ylpropyl)-5-nitro-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-yl]vinyl}phenoxy)acetic acid (0.76 g, 100%) as a yellow solid.

b) To a stirred solution of the above compound (0.76 g, 1.60 mmol) in formic acid (15 mL) was slowly added sodium dithionite (1.64 g, 8.00 mmol) and the mixture was refluxed overnight. The solvent was evaporated under reduced pressure, the residue was redissolved in a mixture of dichloromethane and methanol and the insoluble salts were separated by filtration. The filtrates were acidified until pH 3 by adding dioxane saturated with hydrochloric acid, the solvent was evaporated under reduced pressure and the residue was triturated with a mixture of dichloromethane-diethyl ether, to yield the title compound as a dark yellow solid (0.70 g, 99%).

δ ^{1}H NMR ($CDCl_3$): 9.8 (s, 1H), 7.8 (d, 2H), 6.9 (d, 2H), 6.6 (s, 1H), 4.6 (s, 2H), 3.9 (t, 2H), 3.6 (m, 4H), 3.3 (s, 3H), 2.3 (m, 6H), 1.8 (m, 2H).

PREPARATION 29

6-(4-Hydroxymethylphenyl)-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

a) To a solution of 6-methyl-5-nitro-1,3-dimethyl-1*H*-pyrimidine-2,4-dione (1.59 g, 7.99 mmol) in dry dioxane (50 mL) was added piperidine (1.18 mL, 11.99 mmol), 4-formylbenzoic acid (1.44 g, 7.99 mmol) and 3 A molecular sieves. The mixture was stirred at 50 °C for 5 hours. The resulting solution was concentrated under vacuum and the residue was treated with ethyl acetate, washed with 10% aqueous hydrochloric acid (3 x 50 mL) and brine (3 x 50 mL), dried (Na_2SO_4) and evaporated under reduced pressure. The obtained residue was crystalized from ethanol to yield 4-[2-(1,3-dimethyl-5-nitro-2,6-dioxo-1,2,3,6-tetrahydropyrimidin-4-yl)vinyl]benzoic acid (1.89 g, 70%) as a yellow solid.

b) To a stirred solution of the above compound (0.50 g, 1.51 mmol) in formic acid (15 mL) was slowly added sodium dithionite (1.84 g, 10.56 mmol) and the mixture was refluxed for 24 hours. The resulting solution was cooled to room temperature and poured into water. The resulting precipitate was collected by filtration, washed with water and dried under vacuum to yield 4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzoic acid (0.37 g, 80%) as a white solid.

c) To a stirred solution of the above compound (0.20 g, 0.66 mmol) in dry tetrahydrofuran (3 mL) at 0°C and under argon atmosphere, was slowly added a 1 M solution of borane in tetrahydrofuran (6.67 mL, 6.67 mmol) and the mixture was refluxed for 24 hours. The resulting solution was cooled to room temperature, methanol was slowly added and the solvent was evaporated under reduced pressure. The residue was suspended in ethyl acetate (100 mL), washed with 10% aqueous sodium hydroxide (2 x 10 mL) and water (10 mL). The organic layer was dried (Na_2SO_4) and evaporated under reduced pressure. The obtained residue was crystalized from a mixture of dietyl ether and methanol to yield the title compound (0.080 g, 40%) as a white solid.

δ ^{1}H NMR ($CDCl_3$): 12.3 (bs, 1H), 7.8 (d, 2H), 7.3 (d, 2H), 6.7 (s, 1H), 5.2 (t, 1H), 4.5 (d, 2H), 3.4 (s, 3H), 3.2 (s, 3H).

PREPARATION 30

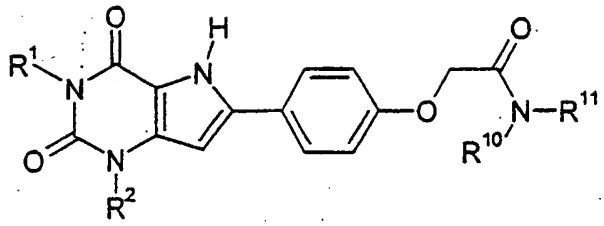
6-(4-Hydroxymethylphenyl)-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

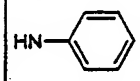
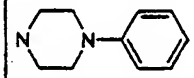
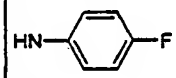
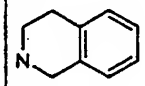
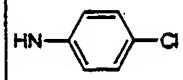
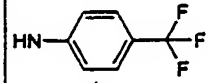
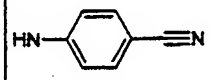
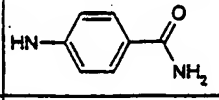
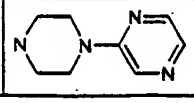
Obtained as a white solid (65% overall) from the title compound of Preparation 26 following the procedure described in Preparation 29c.

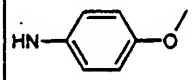
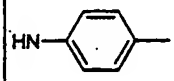
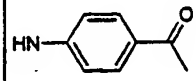
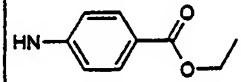
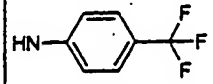
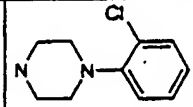
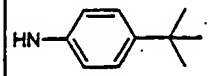
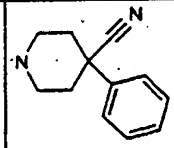
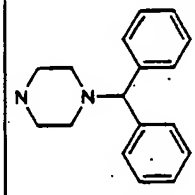
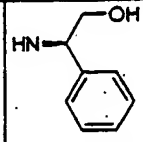
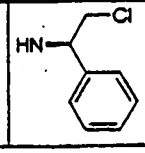
δ ^{1}H NMR ($CDCl_3$): 12.2 (bs, 1H), 7.7 (d, 2H), 7.2 (d, 2H), 6.7 (d, 1H), 5.12 (m, 1H), 4.4(d, 2H), 3.7 (m, 4H), 1.4-1.55 (m, 4H), 0.65-0.8 (m, 6H).

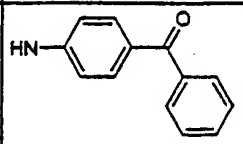
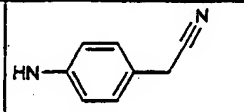
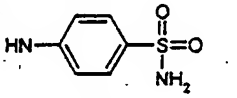
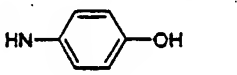
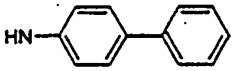
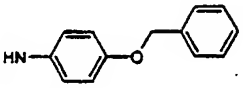
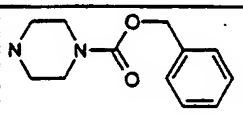
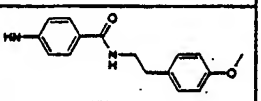
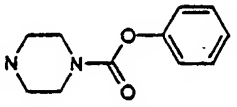
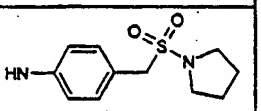
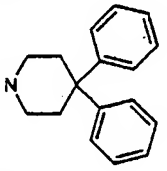
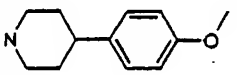
EXAMPLES

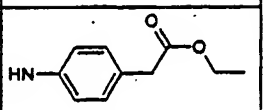
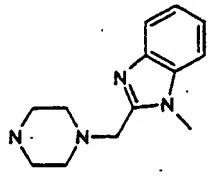
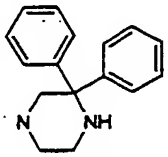
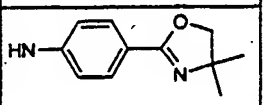
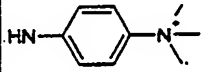
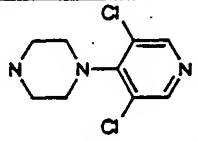
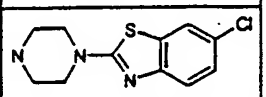
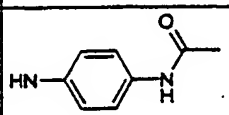
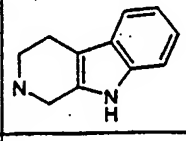
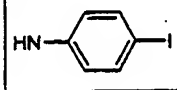
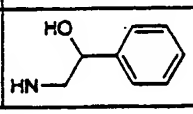
TABLE 3

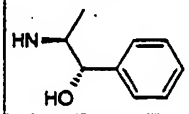
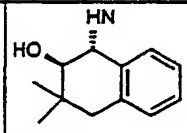
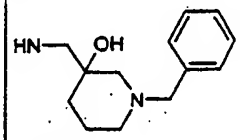
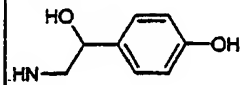
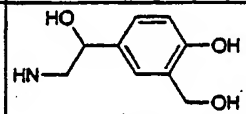
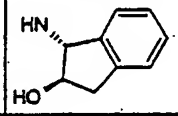
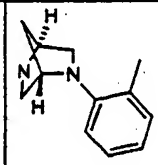
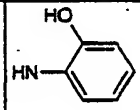
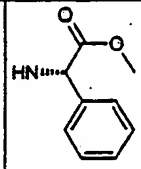
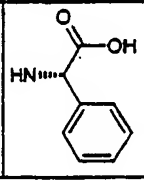


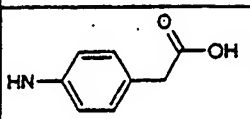
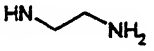
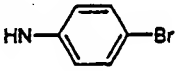
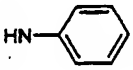
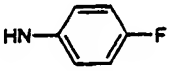
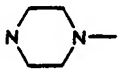
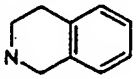
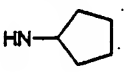
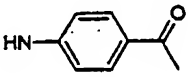
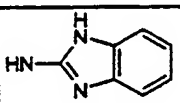
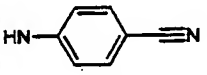
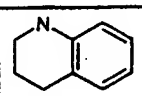
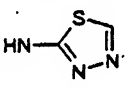
Example No	R^1	R^2	$NR^{10}R^{11}$
1	*n*Pr	*n*Pr	
2	*n*Pr	*n*Pr	
3	*n*Pr	*n*Pr	
4	*n*Pr	*n*Pr	
5	*n*Pr	*n*Pr	
6	*n*Pr	*n*Pr	
7	*n*Pr	*n*Pr	
8	*n*Pr	*n*Pr	
9	*n*Pr	*n*Pr	

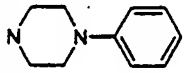
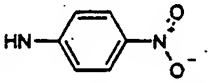
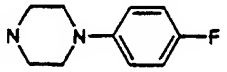
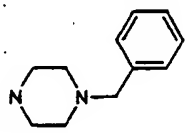
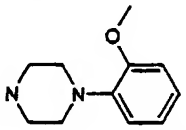
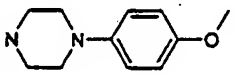
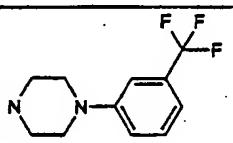
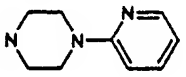
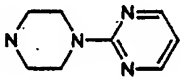
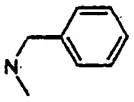
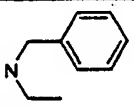
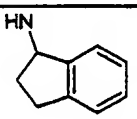
Example No	R^1	R^2	$NR^{10}R^{11}$
10	*n*Pr	*n*Pr	
11	*n*Pr	*n*Pr	
12	*n*Pr	*n*Pr	
13	*n*Pr	*n*Pr	
14	*n*Pr	*n*Pr	
15	*n*Pr	*n*Pr	
16	*n*Pr	*n*Pr	
17	*n*Pr	*n*Pr	
18	*n*Pr	*n*Pr	
19	*n*Pr	*n*Pr	
20	*n*Pr	*n*Pr	

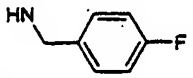
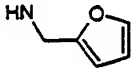
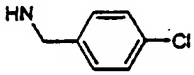
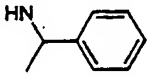
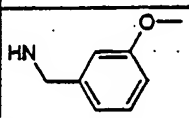
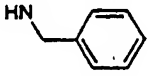
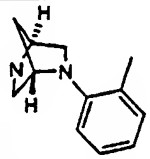
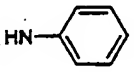
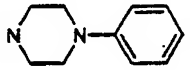
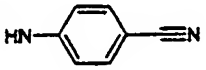
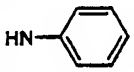
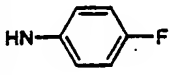
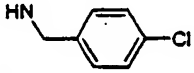
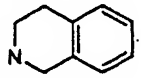
Example No	R^1	R^2	$NR^{10}R^{11}$
21	*n*Pr	*n*Pr	
22	*n*Pr	*n*Pr	
23	*n*Pr	*n*Pr	
24	*n*Pr	*n*Pr	
25	*n*Pr	*n*Pr	
26	*n*Pr	*n*Pr	
27	*n*Pr	*n*Pr	
28	*n*Pr	*n*Pr	
29	*n*Pr	*n*Pr	
30	*n*Pr	*n*Pr	
31	*n*Pr	*n*Pr	
32	*n*Pr	*n*Pr	

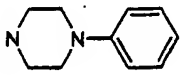
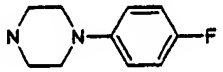
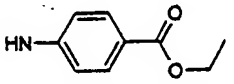
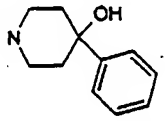
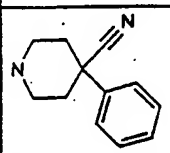
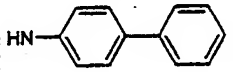
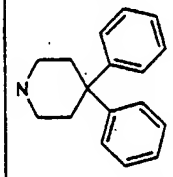
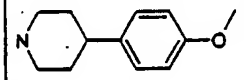
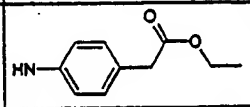
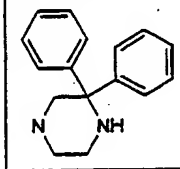
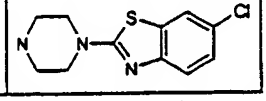
Example No	R^1	R^2	$NR^{10}R^{11}$
33	*n*Pr	*n*Pr	
34	*n*Pr	*n*Pr	
35	*n*Pr	*n*Pr	
36	*n*Pr	*n*Pr	
37	*n*Pr	*n*Pr	
38	*n*Pr	*n*Pr	
39	*n*Pr	*n*Pr	
40	*n*Pr	*n*Pr	
41	*n*Pr	*n*Pr	
42	*n*Pr	*n*Pr	
43	*n*Pr	*n*Pr	

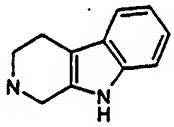
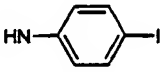
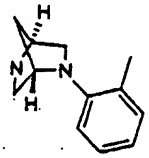
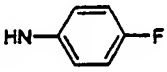
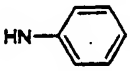
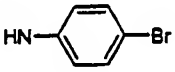
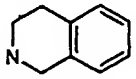
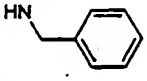
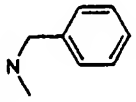
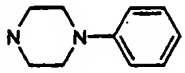
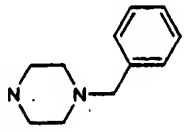
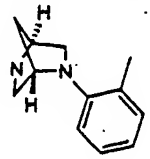
Example No	R^1	R^2	$NR^{10}R^{11}$
44	*n*Pr	*n*Pr	
45	*n*Pr	*n*Pr	
46	*n*Pr	*n*Pr	
47	*n*Pr	*n*Pr	
48	*n*Pr	*n*Pr	
49	*n*Pr	*n*Pr	
50	*n*Pr	*n*Pr	
51	*n*Pr	*n*Pr	
52	*n*Pr	*n*Pr	
53	*n*Pr	*n*Pr	

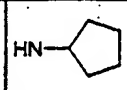
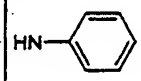
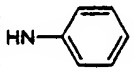
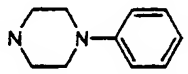
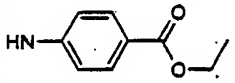
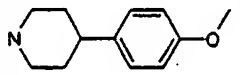
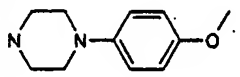
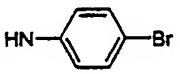
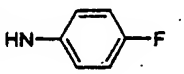
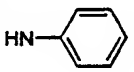
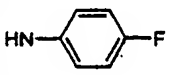
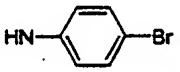
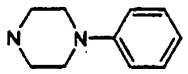
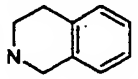
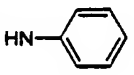
Example No	R^1	R^2	$NR^{10}R^{11}$
54	*n*Pr	*n*Pr	
55	Me	Me	
56	Me	Me	
57	Me	Me	
58	Me	Me	
59	Me	Me	
60	Me	Me	
61	Me	Me	
62	Me	Me	
63	Me	Me	
64	Me	Me	
65	Me	Me	
66	Me	Me	
67	Me	Me	

Example No	R^1	R^2	$NR^{10}R^{11}$
68	Me	Me	
69	Me	Me	
70	Me	Me	
71	Me	Me	
72	Me	Me	
73	Me	Me	
74	Me	Me	
75	Me	Me	
76	Me	Me	
77	Me	Me	
78	Me	Me	
79	Me	Me	

Example No	R^1	R^2	$NR^{10}R^{11}$
80	Me	Me	
81	Me	Me	
82	Me	Me	
83	Me	Me	
84	Me	Me	
85	Me	Me	
86	Me	Me	
87	Et	Et	
88	Et	Et	
89	Et	Et	
90	*n*Pr	Me	
91	*n*Pr	Me	
92	*n*Pr	Me	
93	*n*Pr	Me	

Example No	R^1	R^2	$NR^{10}R^{11}$
94	*n*Pr	Me	
95	*n*Pr	Me	
96	*n*Pr	Me	
97	*n*Pr	Me	
98	*n*Pr	Me	
99	*n*Pr	Me	
100	*n*Pr	Me	
101	*n*Pr	Me	
102	*n*Pr	Me	
103	*n*Pr	Me	
104	*n*Pr	Me	

Example No	R^1	R^2	$NR^{10}R^{11}$
105	*n*Pr	Me	
106	*n*Pr	Me	
107	*n*Pr	Me	
108	Me	*n*Pr	
109	Me	*n*Pr	
110	Me	*n*Pr	
111	Me	*n*Pr	
112	Me	*n*Pr	
113	Me	*n*Pr	
114	Me	*n*Pr	
115	Me	*n*Pr	
116	Me	*n*Pr	

Example No	R^1	R^2	$NR^{10}R^{11}$
117	Me	MeOPro	
118	Me	MeOPro	
119	*i*-Bu	Me	
120	*i*-Bu	Me	
121	H	*n*Pr	
122	H	*n*Pr	
123	H	*n*Pr	
124	H	*n*Pr	
125	H	*n*Pr	
126	MeOEt	MeOEt	
127	MeOEt	MeOEt	
128	MeOEt	MeOEt	
129	MeOEt	MeOEt	
130	MeOEt	MeOEt	
131			

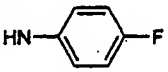
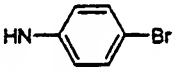
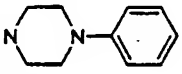
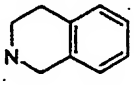
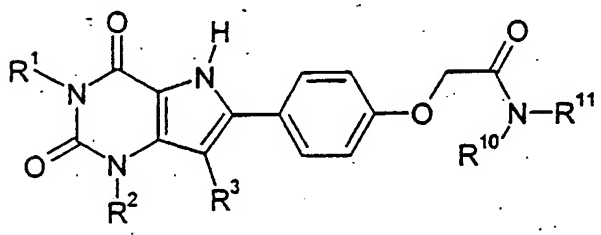
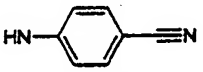
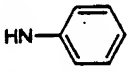
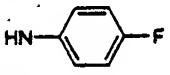
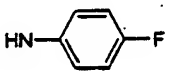
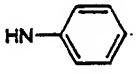
Example No	R^1	R^2	$NR^{10}R^{11}$
132			
133			
134			
135			

TABLE 4



Example No	R^1	R^2	R^3	$NR^{10}R^{11}$
136	Me	Me	Cl	
137	*n*Pr	*n*Pr	Br	
138	*n*Pr	*n*Pr	Br	
139	*n*Pr	*n*Pr	Cl	
140	*n*Pr	*n*Pr	Cl	

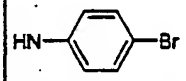
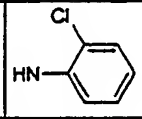
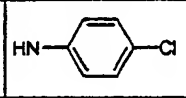
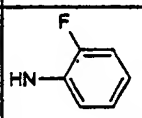
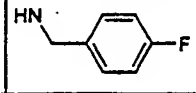
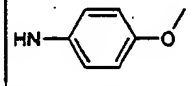
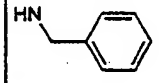
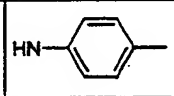
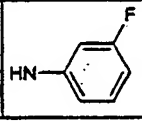
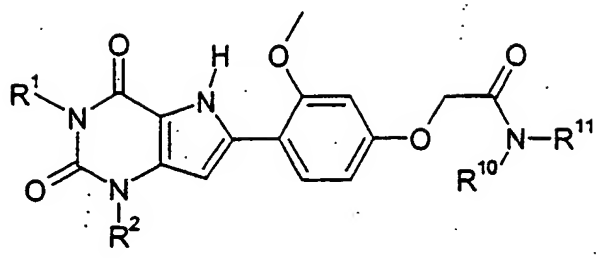
Example No	R^1	R^2	R^3	$NR^{10}R^{11}$
141	*n*Pr	*n*Pr	Cl	
142	*n*Pr	*n*Pr	Cl	
143	*n*Pr	*n*Pr	Cl	
144	*n*Pr	*n*Pr	Cl	
145	*n*Pr	*n*Pr	Cl	
146	*n*Pr	*n*Pr	Cl	
147	*n*Pr	*n*Pr	Cl	
148	*n*Pr	*n*Pr	Cl	
149	*n*Pr	*n*Pr	Cl	

TABLE 5



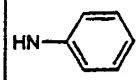
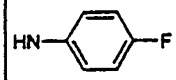
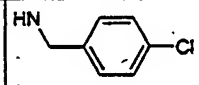
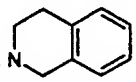
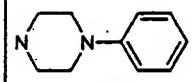
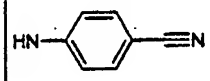
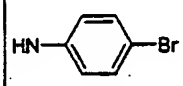
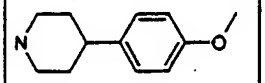
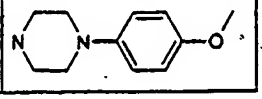
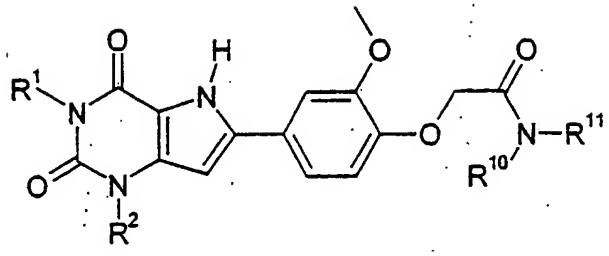
Example No	R^1	R^2	$NR^{10}R^{11}$
150	Me	Me	
151	Me	Me	
152	Me	Me	
153	Me	Me	
154	Me	Me	
155	Me	Me	
156	Me	Me	
157	Me	Me	
158	Me	Me	

TABLE 6



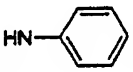
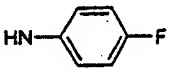
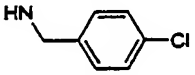
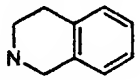
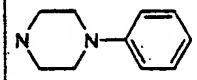
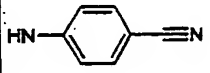
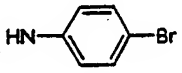
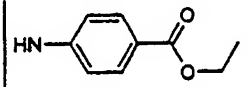
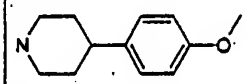
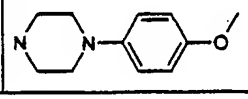
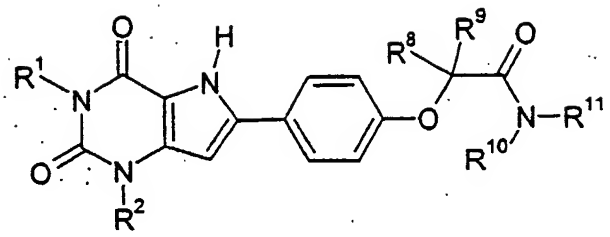
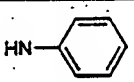
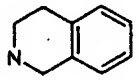
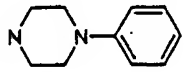
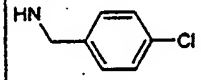
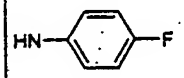
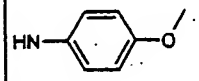
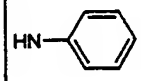
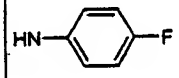
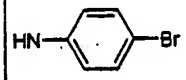
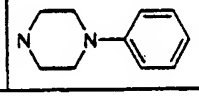
Example No	R^1	R^2	$NR^{10}R^{11}$
159	Me	Me	
160	Me	Me	
161	Me	Me	
162	Me	Me	
163	Me	Me	
164	Me	Me	
165	Me	Me	
166	Me	Me	
167	Me	Me	
168	Me	Me	

TABLE 7



Example No	R^1	R^2	R^8	R^9	$NR^{10}R^{11}$
169	*n*Pr	*n*Pr	H	Me	
170	*n*Pr	*n*Pr	H	Me	
171	*n*Pr	*n*Pr	H	Me	
172	*n*Pr	*n*Pr	H	Me	
173	*n*Pr	*n*Pr	H	Me	
174	*n*Pr	*n*Pr	H	Me	
175	Me	Me	H	Me	
176	Me	Me	H	Me	
177	Me	Me	H	Me	
178	Me	Me	H	Me	

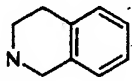
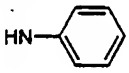
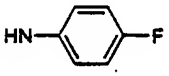
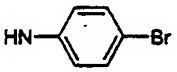
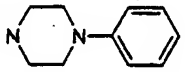
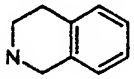
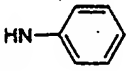
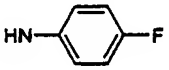
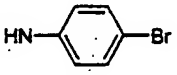
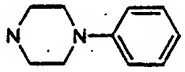
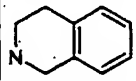
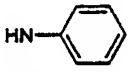
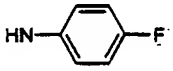
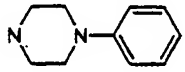
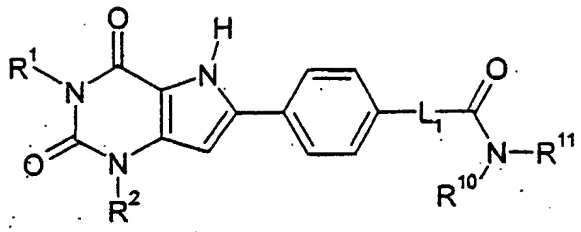
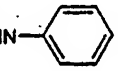
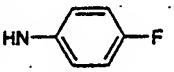
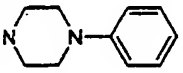
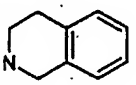
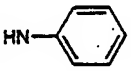
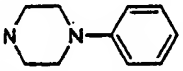
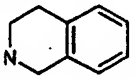
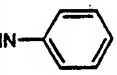
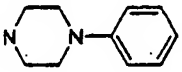
Example No	R^1	R^2	R^8	R^9	$NR^{10}R^{11}$
179	Me	Me	H	Me	
180	*n*Pr	*n*Pr	H	Et	
181	*n*Pr	*n*Pr	H	Et	
182	*n*Pr	*n*Pr	H	Et	
183	*n*Pr	*n*Pr	H	Et	
184	*n*Pr	*n*Pr	H	Et	
185	*n*Pr	*n*Pr	Me	Me	
186	*n*Pr	*n*Pr	Me	Me	
187	*n*Pr	*n*Pr	Me	Me	
188	*n*Pr	*n*Pr	Me	Me	
189	*n*Pr	*n*Pr	Me	Me	
190	*n*Pr	*n*Pr	H	Phe	
191	*n*Pr	*n*Pr	H	Phe	
192	*n*Pr	*n*Pr	H	Phe	

TABLE 8



Example No	R^1	R^2	L_1	$NR^{10}R^{11}$
193	*n*Pr	*n*Pr	$-CH_2CH_2-$	
194	*n*Pr	*n*Pr	$-CH_2CH_2-$	
195	*n*Pr	*n*Pr	$-CH_2CH_2-$	
196	*n*Pr	*n*Pr	$-CH_2CH_2-$	
197	*n*Pr	*n*Pr	-CH=CH-	
198	*n*Pr	*n*Pr	-CH=CH-	
199	*n*Pr	*n*Pr	-CH=CH-	
200	*n*Pr	*n*Pr	$-O(CH_2)_3-$	
201	*n*Pr	*n*Pr	$-O(CH_2)_3-$	
202	*n*Pr	*n*Pr	$-O(CH_2)_3-$	

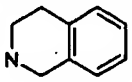
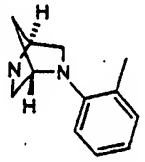
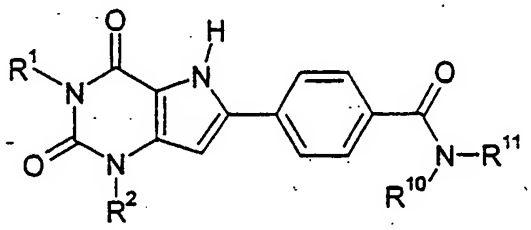
Example No	R^1	R^2	L_1	$NR^{10}R^{11}$
203	*n*Pr	*n*Pr	$-O(CH_2)_3-$	
204	*n*Pr	*n*Pr	$-O(CH_2)_3-$	

TABLE 9



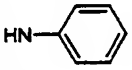
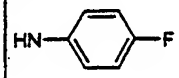
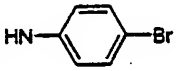
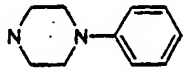
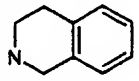
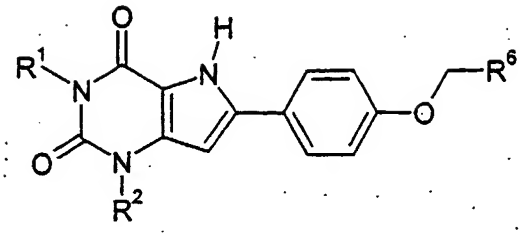
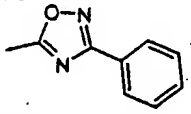
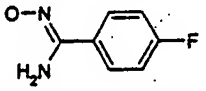
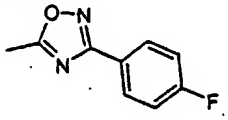
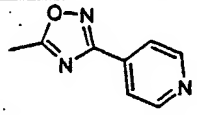
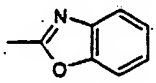
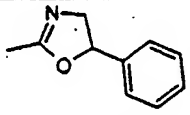
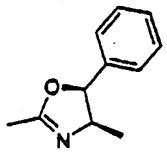
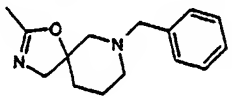
Example No	R^1	R^2	$NR^{10}R^{11}$
205	*n*Pr	*n*Pr	
206	*n*Pr	*n*Pr	
207	*n*Pr	*n*Pr	
208	*n*Pr	*n*Pr	
209	*n*Pr	*n*Pr	

TABLE 10



Example No	R^1	R^2	R^6
210	*n*Pr	*n*Pr	
211	*n*Pr	*n*Pr	
212	*n*Pr	*n*Pr	
213	*n*Pr	*n*Pr	
214	*n*Pr	*n*Pr	
215	*n*Pr	*n*Pr	
216	*n*Pr	*n*Pr	
217	*n*Pr	*n*Pr	

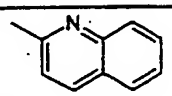
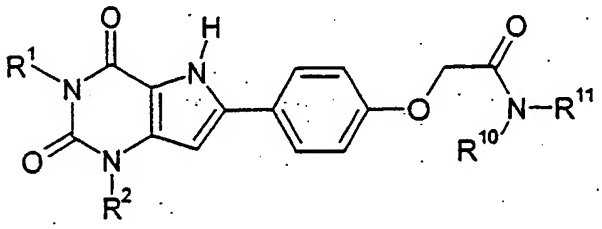
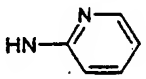
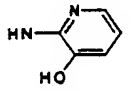
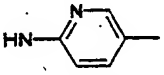
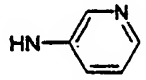
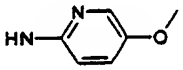
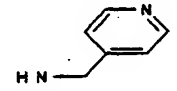
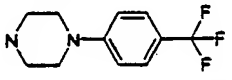
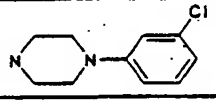
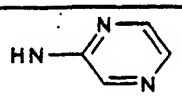
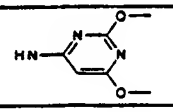
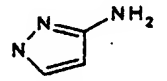
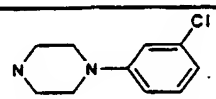
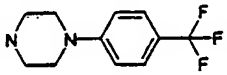
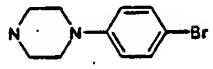
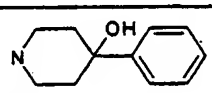
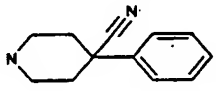
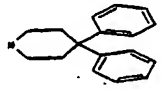
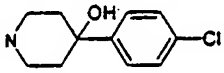
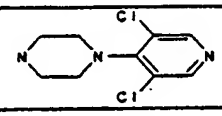
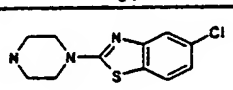
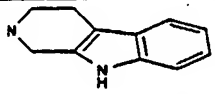
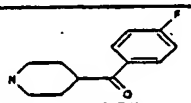
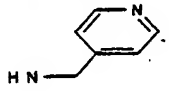
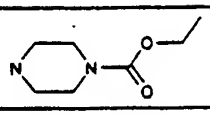
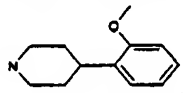
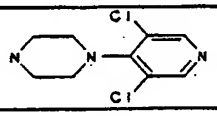
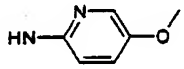
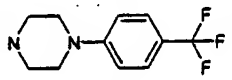
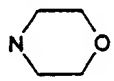
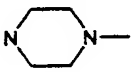
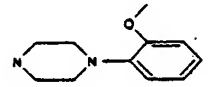
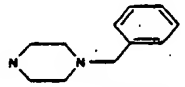
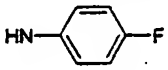
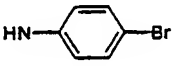
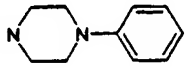
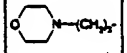
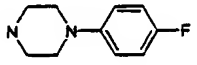
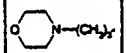
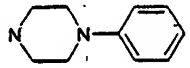
Example No	R^1	R^2	R^6
218	*n*Pr	*n*Pr	

TABLE 11



Example No	R^1	R^2	$NR^{10}R^{11}$
219	*N*Pr	*n*Pr	
220	*n*Pr	*n*Pr	
221	*n*Pr	*n*Pr	
222	*n*Pr	*n*Pr	
223	*n*Pr	*n*Pr	
224	*n*Pr	*n*Pr	
225	*n*Pr	*n*Pr	
226	*n*Pr	*n*Pr	

Example No	R^1	R^2	$NR^{10}R^{11}$
227	*n*Pr	*n*Pr	
228	*n*Pr	*n*Pr	
229	*n*Pr	*n*Pr	
230	Me	Me	
231	Me	Me	
232	Me	Me	
233	Me	Me	
234	Me	Me	
235	Me	Me	
236	Me	Me	
237	Me	Me	
238	Me	Me	
239	Me	Me	
240	Me	Me	
241	Me	Me	

Example No	R^1	R^2	$NR^{10}R^{11}$
242	Me	Me	
243	*n*Pro	Me	
244	*n*Pro	Me	
245	*n*Pro	Me	
246	*n*Pro	Me	
247	*n*Pro	H	
248	*n*Pro	H	
249	*n*Pro	H	
250	*n*Pro	H	
251	*n*Pro	H	
252	*n*Pro	H	
253	*n*Pro	H	
254	H	*n*Pro	
255	Me		
256	Me		

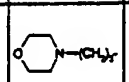
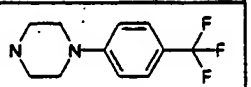
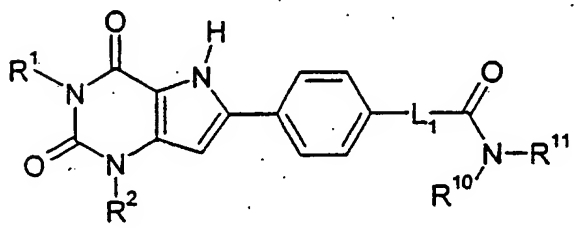
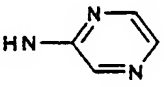
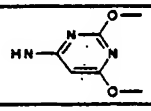
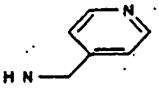
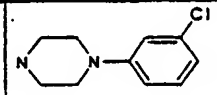
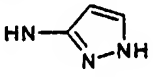
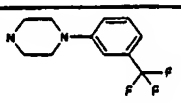
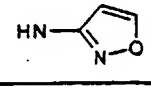
Example No	R^1	R^2	$NR^{10}R^{11}$
257	Me		

TABLE 12



Example No	R^1	R^2	L_1	$NR^{10}R^{11}$
258	*n*Pr	*n*Pr	$-CH_2O-$	
259	*n*Pr	*n*Pr	$-CH_2O-$	
260	*n*Pr	*n*Pr	$-CH_2O-$	
261	*n*Pr	*n*Pr	$-CH_2O-$	
262	*n*Pr	*n*Pr	$-CH_2O-$	
263	*n*Pr	*n*Pr	$-CH_2O-$	
264	*n*Pr	*n*Pr	$-CH_2O-$	

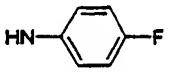
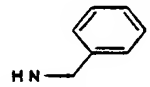
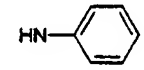
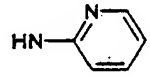
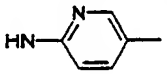
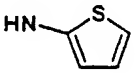
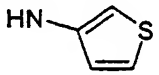
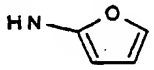
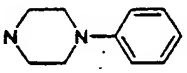
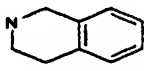
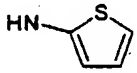
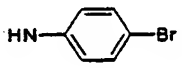
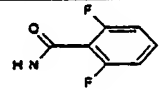
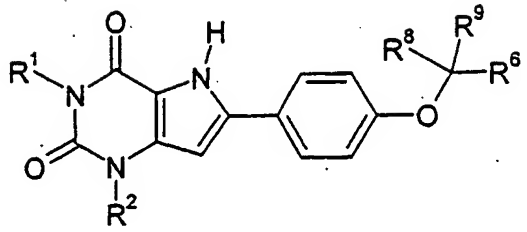
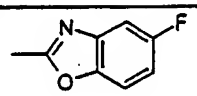
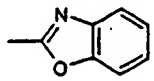
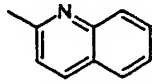
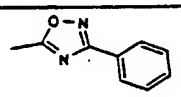
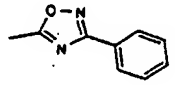
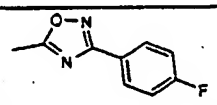
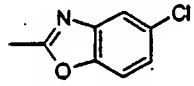
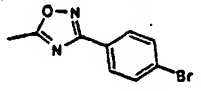
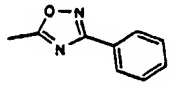
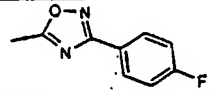
Example No	R^1	R^2	L_1	$NR^{10}R^{11}$
265	Me	Me	$-CH_2O-$	
266	Me	Me	$-CH_2O-$	
267	Me	Me	$-CH_2O-$	
268	Me	Me	$-CH_2O-$	
269	Me	Me	$-CH_2O-$	
270	Me	Me	$-CH_2O-$	
271	Me	Me	$-CH_2O-$	
272	Me	Me	$-CH_2O-$	
273	Me	Me	$-CH_2O-$	
274	Me	Me	$-CH_2O-$	
275	*n*Pr	*n*Pr	$-O(CH_2)_2O-$	
276	*n*Pr	*n*Pr	$-O(CH_2)_2O-$	
277	*n*Pr	*n*Pr	$-CH_2NH-$	

TABLE 13



Example No	R^1	R^2	R^8	R^9	R^6
278	*n*Pr	*n*Pr	H	H	
279	*n*Pr	*n*Pr	H	H	
280	Me	Me	H	H	
281	Me	Me	H	H	
282	*n*Pr	Me	H	H	
283	*n*Pr	Me	H	H	
284	*n*Pr	Me	H	H	
285	*n*Pr	H	H	H	
286	Me	Me	H	Me	
287	Me	Me	H	Me	

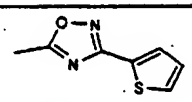
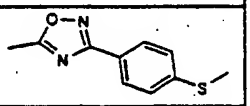
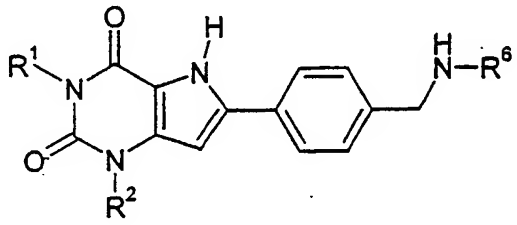
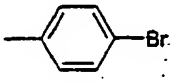
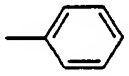
Example No	R^1	R^2	R^8	R^9	R^6
288	Me	Me	H	Me	
289	Me	Me	H	Me	

TABLE 14



Example No	R^1	R^2	R^6
290	*n*Pr	*n*Pr	
291	*n*Pr	*n*Pr	

EXAMPLE 1

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-phenylacetamide

a) To a solution of the title compound of Preparation 1 (300 mg, 0.72 mmol) in anhydrous tetrahydrofuran (20 mL) under argon atmosphere was slowly added at –40°C *N*-methylmorpholine (0.079 mL, 0.72 mmol) and isobutyl chloroformate (0.093 mL, 0.72 mmol). The mixture was stirred at –40°C for 2 hours. Then aniline was added (0.066 mL, 0.72 mmol) and the mixture was stirred 15 minutes at –40°C and 12 hours at

room temperature. The resulting solution was evaporated under reduced pressure and the residue was partitioned between dichloromethane and a saturated aqueous solution of sodium bicarbonate. The organic phase was separated, washed with water and brine, dried (Na_2SO_4) and evaporated under reduced pressure. The resulting crude was purified by flash column chromatography on silica-gel (dichloromethane) to yield the intermediate amide as a yellow solid (150 mg, 42%).

m.p.(EtOH): 62-64°C

δ ^{1}H NMR ($CDCl_3$): 8.18 (bs, 1H), 7.59 (d, 2H), 7.46 (d, 2H), 7.12 (m, 5H), 6.53 (d, 1H), 4.66 (s, 2H), 3.91 (m, 4H), 1.68 (m, 4H), 0.97 (m, 6H).

ESI/MS (m/e,%): 492 (M^+, 46).

b) A stirred solution of the above compound (150 mg, 0.305 mmol) in triethylphosphite (2 mL) was refluxed under argon atmosphere for 5 hours. The mixture was cooled to room temperature and the resulting precipitate was collected by filtration, washed with ethyl ether and dried under vacuum to yield the title compound (65 mg, 46%) as a white solid.

m.p.(MeOH/H_2O): 257-259°C

δ ^{1}H NMR (DMSO): 12.20 (s, 1H), 10.10 (s, 1H), 7.87 (d, 2H), 7.63 (d, 2H), 7.32 (m, 2H), 7.07 (m, 3H), 6.65 (s, 1H), 4.75 (s, 2H), 3.85 (m, 4H), 1.61 (m, 4H), 0.88 (m, 6H).

ESI/MS (m/e,%): 460 (M^+, 100).

EXAMPLE 2

6-{4-[2-Oxo-2-(4-phenylpiperazin-1-yl)ethoxy]phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

Obtained as a white solid (20%) from the title compound of Preparation 1 and 1-phenylpiperazine following the procedure of example 1.

m.p.(MeOH/H_2O): 180-184°C

δ ^{1}H NMR (DMSO): 12.15 (s, 1H), 7.86 (d, 2H), 7.25 (m, 2H), 7.00 (m, 4H), 6.83 (m, 1H), 6.66 (s, 1H), 4.96 (s, 2H), 3.87 (m, 4H), 3.63 (m, 4H), 3.21 (m, 2H), 3.14

(m, 2H), 2.51 (m, 4H), 0.90 (m, 6H).

ESI/MS (m/e,%): 529 (M^+, 19).

EXAMPLE 3

2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(4-fluorophenyl) acetamide

Obtained as a white solid (23%) from the title compound of Preparation 1 and 4-fluoroaniline following the procedure of example 1.

m.p.($MeOH/H_2O$): 256-258°C

δ ^1H NMR (DMSO): 12.21 (s, 1H), 10.18 (s, 1H), 7.89 (m, 2H), 7.63 (m, 2H), 7.12 (m, 4H), 6.67 (s, 1H), 4.77 (s, 2H), 3.84 (m, 4H), 1.61 (m, 4H), 0.91 (m, 6H).

ESI/MS (m/e,%): 478 (M^+, 100).

EXAMPLE 4

6-{4-[2-(3,4-Dihydro-1*H*-isoquinolin-2-yl)-2-oxoethoxy] phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

To mixture of the title compound of Preparation 2 (480 mg, 1.24 mmol), *N*-(3-dimethylaminopropyl)-*N'*-ethyl carbodiimide hydrochloride (285 mg, 1.49 mmol), 1-hydroxybenzotriazole (201 mg, 1.49 mmol) and triethylamine (0.44 mL, 2.48 mmol) in dimethylformamide (20 mL) was added 1,2,3,4-tetrahydroisoquinoline (0.205 mL, 1.61 mmol) and the mixture was stirred at room temperature overnight. The resulting solution was evaporated under reduced pressure and the residue was partitioned between dichloromethane and a saturated aqueous solution of sodium bicarbonate. The organic phase was separated, washed with water and brine, dried (Na_2SO_4) and evaporated under reduced pressure. The resulting crude was purified by flash column chromatography on silica-gel (hexanes:ethyl acetate 1:1) to yield the title compound as a white solid (270 mg, 43%).

m.p.: 176.9-177.6°C

δ ^1H NMR (DMSO): 12.22 (bs, 1H), 7.83 (d, 2H), 7.20 (m, 4H), 7.00 (d, 2H),

6.65 (s, 1H), 4.98 (s, 2H), 4.67 (m, 2H), 3.85 (m, 4H), 3.70 (m, 2H), 2.86 (m, 2H), 1.65 (m, 4H), 0.89 (m, 6H).

ESI/MS (m/e,%): 500 (M^+, 82).

EXAMPLE 5

_N_-(4-Chlorophenyl)-2-[4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1_H_-pyrrolo[3,2-_d_]pyrimidin-6-yl)phenoxy] acetamide

To mixture of the title compound of Preparation 2 (80 mg, 0.21 mmol), _N_-(3-dimethylaminopropyl)-_N'_-ethylcarbodiimide hydrochloride (44 mg, 0.23 mmol), 1-hydroxybenzotriazole (31 mg, 0.23 mmol) and polymer bound morpholine (280 mg, 2.75 mmol/g based on nitrogen analysis) in dimethylformamide (4 mL) was added 4-chloroaniline (32 mg, 0.25 mmol) and the mixture was stirred at room temperature overnight. To the resulting suspension was added macroporous triethylammonium methylpolystyrene carbonate (250 mg, 2.8-3.5 mmol/g based on nitrogen elemental analysis) and Amberlyst 15 (650 mg) as scavengers and stirred for 2 hours (in case of acidic or basic final products the corresponding scavenger was not added). The resulting suspension was filtered and evaporated under reduced pressure. The residue was triturated with a mixture of MeOH:ethyl ether and the precipitate collected by filtration to yield the title compound as a white solid (80 mg, 78%).

ESI/MS m/e: 495 ($[M+H]^+$, $C_{26}H_{27}ClN_4O_4$).

Retention Time (min.): 11.0

EXAMPLE 6-53

The compounds of this invention were synthesized from the title compound of Preparation 2 following the procedure of example 5 and using the corresponding reactant respectively. The ESI/MS data, HPLC retention times and yields are summarised in the following table.

TABLE 15

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
6	$C_{27}H_{27}F_3N_4O_5$	545	11.1	35
7	$C_{27}H_{27}N_5O_4$	486	10.2	60
8	$C_{27}H_{29}N_5O_5$	504	9.1	48
9	$C_{28}H_{33}N_7O_4$	532	9.5	57
10	$C_{27}H_{30}N_4O_5$	491	10.3	76
11	$C_{27}H_{30}N_4O_4$	475	10.7	38
12	$C_{28}H_{30}N_4O_5$	503	10.1	64
13	$C_{29}H_{32}N_4O_6$	533	10.8	52
14	$C_{27}H_{27}F_3N_4O_4$	529	11.1	75
15	$C_{30}H_{34}ClN_5O_4$	564	11.2	37
16	$C_{30}H_{36}N_4O_4$	517	11.5	45
17	$C_{32}H_{35}N_5O_4$	554	10.6	55
18	$C_{37}H_{41}N_5O_4$	620	11.5	40
19	$C_{28}H_{32}N_4O_5$	505	9.7	93
20	$C_{28}H_{31}ClN_4O_4$	524	10.6	73
21	$C_{33}H_{32}N_4O_5$	565	11.0	80
22	$C_{28}H_{29}N_5O_4$	500	9.9	63
23	$C_{26}H_{29}N_5O_6S$	540	9.3	50
24	$C_{26}H_{28}N_4O_5$	477	9.5	28
25	$C_{32}H_{32}N_4O_4$	537	11.4	61
26	$C_{33}H_{34}N_4O_5$	567	11.2	41
27	$C_{32}H_{37}N_5O_6$	588	10.5	39

28	$C_{36}H_{39}N_5O_6$	638	10.5	64
29	$C_{31}H_{35}N_5O_6$	574	10.3	39
30	$C_{31}H_{37}N_5O_6S$	608	10.1	76
31	$C_{37}H_{40}N_4O_4$	605	11.5	66
32	$C_{32}H_{38}N_4O_5$	559	10.9	39
33	$C_{30}H_{34}N_4O_6$	547	10.6	47
34	$C_{33}H_{39}N_7O_4$	598	8.4	70
35	$C_{36}H_{39}N_5O_4$	606	9.7	71
36	$C_{31}H_{35}N_5O_5$	558	10.3	65
37	$C_{29}H_{36}N_5O_4$	519	7.0	44
38	$C_{29}H_{32}Cl_2N_6O_4$	599	10.7	35
39	$C_{31}H_{33}ClN_6O_4S$	621	11.3	56
40	$C_{28}H_{31}N_5O_5$	518	9.4	60
41	$C_{31}H_{33}N_5O_4$	540	10.7	52
42	$C_{26}H_{27}IN_4O_4$	587	11.2	44
43	$C_{28}H_{32}N_4O_5$	505	9.8	62
44	$C_{29}H_{34}N_4O_5$	519	10.1	88
45	$C_{32}H_{35}N_5O_6$	586	10.1	65
46	$C_{33}H_{41}N_5O_5$	588	7.3	79
47	$C_{28}H_{32}N_4O_6$	521	9.0	87
48	$C_{29}H_{34}N_4O_7$	551	8.6	84
49	$C_{29}H_{32}N_4O_5$	517	10.0	63
50	$C_{32}H_{37}N_5O_4$	556	11.0	60
51	$C_{26}H_{28}N_4O_5$	477	10.1	44
52	$C_{29}H_{32}N_4O_6$	533	10.3	91

53	$C_{28}H_{30}N_4O_6$	519	10.2	57
54	$C_{28}H_{30}N_4O_6$	519	9.7	85

EXAMPLE 54

(4-{2-[4-(2,4-Dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]acetylamino}phenyl) acetic acid

To a suspension of the title compound of Example 33 (33 mg, 0.06 mmol) in methanol (0.3 mL) was added NaOH 2N (0.3 mL) and the mixture was heated at 50°C for 1 hour. The mixture was cooled to room temperature and acetic acid was added until acidic pH was observed. The resulting precipitate was collected by filtration and dried to yield the title compound (13 mg, 42%) as a white solid.

ESI/MS m/e: 519 ($[M+H]^+$, $C_{28}H_{30}N_4O_6$).

Retention Time (min.): 9.7

General procedure for the synthesis of examples 55-76

The reaction took place in a sealed tube under argon atmosphere. Usually 50 mg of the title compound of Preparation 3 were used and 2 mL of those amines that are liquid and 160 equivalents of those amines that are solid. In all reactions a catalytic amount of sodium cyanide was added. In case of liquid amines the reaction mixture was heated at the boiling temperature of the amine and in the case of solid amines 2 mL of anhydrous dioxane were added and heated to the boiling point of dioxane. The reactions were followed by TLC and when no more starting material was left, the mixture was cooled to room temperature and usually the final product was isolated by filtration of the corresponding precipitate which was washed with ethyl ether. Occasionally the reaction mixture was concentrated under reduced pressure and the residue chromatographed on silica-gel (dichloromethane:methanol). The title compounds were crystallized in mixtures of MeOH:H_2O.

EXAMPLE 55

N-(2-Aminoethyl)-2-[4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] acetamide

Obtained as a white solid (33%) from the title compound of Preparation 3 and ethylenediamine following the procedure described above.

δ ^{1}H NMR (DMSO): 7.85 (d, 2H), 7.01 (d, 2H), 6.63 (s, 1H), 4.52 (s, 2H), 3.41 (s, 3H), 3.25 (s, 3H), 3.12 (m, 2H), 2.50 (m, 2H).

EXAMPLE 56

N-(4-Bromophenyl)-2-[4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] acetamide

Obtained as a brown solid (15%) from the title compound of Preparation 3 and 4-bromoaniline following the procedure described above.

δ ^{1}H NMR (DMSO): 7.89 (d, 2H), 7.19 (d, 2H), 7.00 (d, 2H), 6.67 (s, 1H), 6.57 (m, 2H), 4.61 (s, 2H), 3.49 (s, 3H), 3.33 (s, 3H).

EXAMPLE 57

2-[4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-phenylacetamide

Obtained as a brown solid (74%) from the title compound of Preparation 3 and aniline following the procedure described above.

m.p.: >300°C

δ ^{1}H NMR (DMSO): 12.30 (bs, 1H), 10.22 (bs, 1H), 7.88 (d, 2H), 7.66 (d, 2H), 7.34 (m, 2H), 7.09 (m, 3H), 6.62 (s, 1H), 4.78 (s, 2H), 3.42 (s, 3H), 3.27 (s, 3H).

ESI/MS (m/e,%): 405 [$(M+1)^+$, 46].

EXAMPLE 58

2-[4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(4-fluorophenyl) acetamide

Obtained as a white solid (10%) from the title compound of Preparation 3 and 4-fluoroaniline following the procedure described above.

m.p.: >300°C

δ ^{1}H NMR (DMSO): 12.50 (bs, 1H), 10.36 (bs, 1H), 8.08 (d, 2H), 7.87 (m, 2H), 7.38 (m, 2H), 7.28 (d, 2H), 6.83 (s, 1H), 5.00 (s, 2H), 3.53 (s, 3H), 3.46 (s, 3H).

ESI/MS (m/e,%): 423 [$(M+1)^+$, 100].

EXAMPLE 59

1,3-Dimethyl-6-{4-[2-(4-methylpiperazin-1-yl)-2-oxo-ethoxy]phenyl}-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

Obtained as a brown solid (72%) from the title compound of Preparation 3 and 1-methylpiperazine following the procedure described above.

m.p.: >275°C

δ ^{1}H NMR (DMSO): 7.84 (d, 2H), 6.97 (d, 2H), 6.57 (s, 1H), 4.88 (s, 2H), 3.42 (s, 3H), 3.27 (s, 3H), 2.51 (m, 2H), 2.35 (m, 2H), 2.27 (m, 2H), 2.13 (m, 2H).

ESI/MS (m/e,%): 412 [$(M+1)^+$, 100].

EXAMPLE 60

1,3-Dimethyl-6-[4-(2-morpholin-4-yl-2-oxoethoxy)phenyl]-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

Obtained as a brown solid (27%) from the title compound of Preparation 3 and morpholine following the procedure described above.

m.p.: >300°C

δ ^{1}H NMR (DMSO): 12.42 (bs, 1H), 8.01 (d, 2H), 7.16 (d, 2H), 6.80 (s, 1H), 5.07 (s, 2H), 3.76 (m, 4H), 3.63 (m, 4H), 3.59 (s, 3H), 3.43 (s, 3H).

ESI/MS (m/e,%): 398 (M^+, 42).

EXAMPLE 61

6-{4-[2-(3,4-Dihydro-1*H*-isoquinolin-2-yl)-2-oxoethoxy] phenyl}-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

Obtained as a white solid (32%) from the title compound of Preparation 3 and 1,2,3,4-tetrahydro isoquinoline following the procedure described above.

m.p.: >280°C

δ ^{1}H NMR (DMSO): 12.14 (bs, 1H), 7.71 (d, 2H), 7.07 (m, 4H), 6.89 (d, 2H), 6.50 (s, 1H), 4.86 (s, 2H), 3.56 (m, 2H), 3.35 (m, 2H), 3.29 (s, 3H), 3.13 (s, 3H), 2.72 (m, 1H), 2.39 (m, 1H).

ESI/MS (m/e,%): 444 (M^+, 34).

EXAMPLE 62

***N*-Cyclopentyl-2-[4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] acetamide**

Obtained as a white solid (81%) from the title compound of Preparation 3 and cyclopentylamine following the procedure described above.

m.p.: >270°C

δ ^{1}H NMR (DMSO): 8.02 (d, 2H), 7.18 (d, 2H), 6.69 (s, 1H), 4.68 (s, 2H), 4.27 (m, 1H), 3.60 (s, 3H), 3.45 (s, 3H), 2.03-1.60 (m, 8H).

ESI/MS (m/e,%): 396 (M^+, 18).

EXAMPLE 63

***N*-(4-Acetylphenyl)-2-[4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] acetamide**

Obtained as a brown solid (24%) from the title compound of Preparation 3 and acetanilide following the procedure described above.

m.p.: >300°C

δ ^{1}H NMR (DMSO): 8.03 (d, 2H), 7.93 (d, 2H), 7.85 (d, 2H), 7.15 (d, 2H), 6.68 (s, 1H), 4.89 (s, 2H), 3.49 (s, 3H), 3.33 (s, 3H), 2.60 (s, 3H).

ESI/MS (m/e,%): 446 (M^+, 35).

EXAMPLE 64

***N*-(1*H*-Benzoimidazol-2-yl)-2-[4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] acetamide**

Obtained as a brown solid (84%) from the title compound of Preparation 3 and 2-aminobenzimidazole following the procedure described above.

m.p.: >287°C (decomposition)

δ ^{1}H NMR (DMSO): 12.12 (bs, 1H), 7.83 (d, 2H), 7.40 (m, 2H), 7.04 (m, 4H), 6.80 (bs, 1H), 6.58 (s, 1H), 6.04 (bs, 1H), 4.88 (s, 2H), 3.38 (s, 3H), 3.22 (s, 3H).

EXAMPLE 65

***N*-(4-Cyanophenyl)-2-[4-(1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy] acetamide**

Obtained as a brown solid (13%) from the title compound of Preparation 3 and 4-aminobenzonitrile following the procedure described above.

m.p.: 263-265°C

δ ^{1}H NMR (DMSO): 12.18 (bs, 1H), 10.50 (bs, 1H), 7.79 (m, 6H), 7.05 (m, 2H), 6.60 (s, 1H), 4.77 (s, 2H), 3.37 (s, 3H), 3.24 (s, 3H).

EXAMPLE 66

6-{4-[2-(3,4-Dihydro-2*H*-quinolin-1-yl)-2-oxoethoxy]phenyl}-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

Obtained as a yellow solid (47%) from the title compound of Preparation 3 and 1,2,3,4-tetrahydroquinoline following the procedure described above.

δ ^{1}H NMR ($CDCl_3$): 11.60 (s, 1H), 7.62 (d, 2H), 7.10 (m, 4H), 6.78 (d, 2H), 5.20 (s, 1H), 4.79 (s, 2H), 3.76 (m, 2H), 3.73 (s, 3H), 3.23 (s, 3H), 2.60 (m, 2H), 1.77 (m, 2H).

EXAMPLE 67

2-[4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-[1,3,4]thiadiazol-2-ylacetamide

Obtained as a brown solid (29%) from the title compound of Preparation 3 and 2-amino-1,3,4-thiadiazole following the procedure described above.

m.p.: >300°C (decomposition)

δ ^{1}H NMR (DMSO): 9.23 (s, 1H), 8.64 (s, 1H), 7.93 (d, 2H), 7.26 (s, 1H), 7.12 (d, 2H), 6.70 (s, 1H), 5.03 (s, 2H), 3.49 (s, 3H), 3.33 (s, 3H).

EXAMPLE 68

1,3-Dimethyl-6-{4-[2-oxo-2-(4-phenylpiperazin-1-yl)ethoxy]phenyl}-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

Obtained as a white solid (20%) from the title compound of Preparation 3 and 1-phenylpiperazine following the procedure described above.

m.p.: >270°C (decomposition)

δ ^{1}H NMR (DMSO): 11.25 (s, 1H), 7.76 (d, 2H), 7.28 (m, 3H), 7.02 (d, 2H), 6.91 (m, 2H), 6.18 (s, 1H), 4.80 (s, 2H), 3.78 (m, 4H), 3.53 (s, 3H), 3.49 (s, 3H), 3.47 (m, 4H).

EXAMPLE 69

2-[4-(1,3-Dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(4-nitrophenyl) acetamide

Obtained as a yellow solid (15% overall) from the title compound of Preparation 1 and 4-nitroaniline following the procedure of example 1.

m.p.: 228-230°C

δ ^{1}H NMR (DMSO): 12.30 (bs, 1H), 10.80 (bs, 1H), 8.31 (d, 2H), 7.95 (m, 4H), 7.13 (d, 2H), 6.69 (s, 1H), 4.91 (s, 2H), 3.51 (s, 3H), 3.31 (s, 3H).

EXAMPLE 70

6-(4-{2-[4-(4-Fluorophenyl)piperazin-1-yl]-2-oxoethoxy} phenyl)-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

Obtained as a white solid (50%) from the title compound of Preparation 3 and 1-(4-fluorophenyl)piperazine following the general procedure described above.

m.p.: >265°C (decomposition)

δ ^{1}H NMR (DMSO): 12.30 (bs, 1H), 7.84 (d, 2H), 7.04 (m, 6H), 6.63 (s, 1H), 4.95 (s, 2H), 3.62 (m, 4H), 3.42 (s, 3H), 3.26 (s, 3H), 3.14 (m, 2H), 3.07 (m, 2H).

ESI/MS (m/e,%): 491 (M^+, 100).

EXAMPLE 71

6-{4-[2-(4-Benzylpiperazin-1-yl)-2-oxoethoxy]phenyl}-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

Obtained as an off-white solid (40%) from the title compound of Preparation 3 and 1-benzylpiperazine following the general procedure described above.

m.p.: 170-172°C

δ ^{1}H NMR (DMSO): 12.05 (bs, 1H), 7.64 (d, 2H), 7.14 (s, 5H), 6.78 (d, 2H), 6.38 (s, 1H), 4.68 (s, 2H), 3.20 (m, 8H), 2.24 (m, 2H), 2.16 (m, 2H).

ESI/MS (m/e,%): 487 (M^+, 100).

EXAMPLE 72

6-(4-{2-[4-(2-Methoxyphenyl)piperazin-1-yl]-2-oxoethoxy} phenyl)-1,3-dimethyl-1,5-dihydro-pyrrolo[3,2-*d*]pyrimidine-2,4-dione

Obtained as a brown solid (83%) from the title compound of Preparation 3 and 1-(2-methoxyphenyl)piperazine following the general procedure described above.

m.p.: >295°C (decomposition)

δ ^{1}H NMR (DMSO): 12.21 (bs, 1H), 7.76 (m, 2H), 6.86 (m, 6H), 6.52 (s, 1H), 4.88 (s, 2H), 3.76 (s, 3H), 3.58 (m, 4H), 3.38 (s, 3H), 3.22 (s, 3H), 2.49 (m, 4H).

ESI/MS (m/e,%): 503 (M^+, 100).

EXAMPLE 73

6-(4-{2-[4-(4-Methoxyphenyl)piperazin-1-yl]-2-oxoethoxy} phenyl)-1,3-dimethyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

Obtained as a white solid (23%) from the title compound of Preparation 3 and 1-(4-methoxyphenyl)piperazine following the general procedure described above.

m.p.: 269-271°C

δ ^{1}H NMR (DMSO): 12.38 (bs, 1H), 7.96 (d, 2H), 7.09 (d, 2H), 7.05 (d, 2H), 6.96 (d, 2H), 6.74 (s, 1H), 5.06 (s, 2H), 3.81 (s, 3H), 3.73 (m, 4H), 3.54 (s, 3H), 3.38 (s, 3H), 3.19 (m, 2H), 3.11 (m, 4H).

ESI/MS (m/e,%): 503 (M^+, 100).

EXAMPLE 74

1,3-Dimethyl-6-(4-{2-oxo-2-[4-(3-trifluoromethylphenyl)piperazin-1-yl]ethoxy}phenyl)-1,5-dihydropyrrolo[3,2-*d*] pyrimidine-2,4-dione

Obtained as a white solid (50%) from the title compound of Preparation 3 and 1-(3-trifluoromethylphenyl) piperazine following the general procedure described above.

m.p.: >275°C (decomposition)

δ ^{1}H NMR (DMSO): 7.77 (m, 2H), 7.40 (m, 1H), 7.28 (m, 2H), 7.15 (d, 1H), 6.94 (m, 3H), 4.88 (s, 2H), 4.65 (s, 1H), 3.68 (s, 3H), 3.30 (m, 11H).

ESI/MS (m/e,%): 541 (M^+, 100).

EXAMPLE 75

1,3-Dimethyl-6-{4-[2-oxo-2-(4-pyridin-2-yl-piperazin-1-yl)ethoxy]phenyl}-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

Obtained as a white solid (42%) from the title compound of Preparation 3 and 1-pyridin-2-ylpiperazine following the general procedure described above.

m.p.: >260°C (decomposition)

δ ^{1}H NMR (DMSO): 8.14 (d, 1H), 7.84 (d, 2H), 7.57 (m, 1H), 7.01 (d, 2H), 6.88

(m, 1H), 6.68 (m, 1H), 6.60 (s, 1H), 4.91 (s, 2H), 3.60-3.26 (m, 14H).

ESI/MS (m/e,%): 474 (M^+, 100).

EXAMPLE 76

1,3-Dimethyl-6-{4-[2-oxo-2-(4-pyrimidin-2-ylpiperazin-1-yl)ethoxy]phenyl}-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

Obtained as a white solid (60%) from the title compound of Preparation 3 and 2-piperazin-1-ylpyrimidine following the general procedure described above.

m.p.: >275°C (decomposition)

δ ^{1}H NMR (DMSO): 12.27 (bs, 1H), 8.41 (d, 2H), 7.85 (d, 2H), 7.03 (d, 1H), 6.69 (t, 1H), 6.63 (s, 1H), 4.96 (s, 2H), 3.83 (m, 2H), 3.76 (m, 2H), 3.57 (m, 4H), 3.43 (s, 3H), 3.27 (s, 3H).

EXAMPLES 77-86

The compounds of this invention were synthesized from the title compound of Preparation 4 following the procedure of example 5 and using the corresponding reactant respectively. The ESI/MS data, HPLC retention times and yields are summarised in the following table.

TABLE 16

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
77	$C_{24}H_{24}N_4O_4$	433	15.3	33
78	$C_{25}H_{26}N_4O_4$	447	16.2	36
79	$C_{25}H_{24}N_4O_4$	445	16.0	37
80	$C_{23}H_{21}FN_4O_4$	437	15.0	30
81	$C_{21}H_{20}N_4O_5$	409	13.6	50
82	$C_{23}H_{21}ClN_4O_4$	452	16.0	55

83	$C_{24}H_{24}N_4O_4$	433	15.5	60
84	$C_{24}H_{24}N_4O_5$	449	14.8	40
85	$C_{23}H_{22}N_4O_4$	419	14.7	43
86	$C_{28}H_{29}N_5O_4$	500	9.5	20

EXAMPLES 87-89

The compounds of this invention were synthesized from the title compound of Preparation 5 following the procedure of example 5 and using the corresponding reactant respectively. The ESI/MS data, HPLC retention times and yields are summarised in the following table.

TABLE 17

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
87	$C_{24}H_{24}N_4O_4$	433	10.6	10
88	$C_{28}H_{31}N_5O_4$	502	10.9	24
89	$C_{25}H_{23}N_5O_4$	458	9.4	35

EXAMPLES 90-107

The compounds of this invention were synthesized from the title compound of Preparation 6 following the procedure of example 5 and using the corresponding reactant respectively. The ESI/MS data, HPLC retention times and yields are summarised in the following table.

TABLE 18

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
90	$C_{24}H_{24}N_4O_4$	433	9.6	51

91	$C_{24}H_{23}FN_4O_4$	450	9.7	48
92	$C_{25}H_{25}ClN_4O_4$	480	10.0	60
93	$C_{27}H_{28}N_4O_4$	473	9.8	45
94	$C_{28}H_{31}N_5O_4$	502	9.9	40
95	$C_{28}H_{30}FN_5O_4$	520	10.0	62
96	$C_{27}H_{28}N_4O_6$	505	10.2	39
97	$C_{29}H_{32}N_4O_5$	517	9.3	47
98	$C_{30}H_{31}N_5O_4$	526	9.9	50
99	$C_{30}H_{28}N_4O_4$	509	10.9	86
100	$C_{35}H_{36}N_4O_4$	577	10.9	88
101	$C_{30}H_{34}N_4O_5$	531	10.3	66
102	$C_{28}H_{30}N_4O_6$	519	9.9	49
103	$C_{34}H_{35}N_5O_4$	578	8.6	65
104	$C_{29}H_{29}ClN_6O_4S$	593	10.8	44
105	$C_{29}H_{29}N_5O_4$	512	10.1	58
106	$C_{24}H_{23}IN_4O_4$	528	10.2	31
107	$C_{30}H_{33}N_5O_4$	620	11.5	44

EXAMPLES 108-116

The compounds of this invention were synthesized from the title compound of Preparation 7 following the procedure of example 5 and using the corresponding reactant respectively. The ESI/MS data, HPLC retention times and yields are summarised in the following table.

TABLE 19

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
108	$C_{24}H_{23}FN_4O_4$	451	10.8	78
109	$C_{24}H_{24}N_4O_4$	433	10.7	65
110	$C_{24}H_{23}BrN_4O_4$	512	11.6	72
111	$C_{27}H_{28}N_4O_4$	473	11.0	99
112	$C_{25}H_{26}N_4O_4$	447	10.5	47
113	$C_{26}H_{28}N_4O_4$	461	10.8	88
114	$C_{28}H_{31}N_5O_4$	502	11.1	73
115	$C_{29}H_{33}N_5O_4$	516	7.8	69
116	$C_{30}H_{33}N_5O_4$	528	10.3	23

EXAMPLE 117

_N_-Cyclopentyl-2-{4-[1-(3-methoxypropyl)-3-methyl-2,4-dioxo-2,3,4,5-tetrahydro-1_H_-pyrrolo[3,2-_d_]pyrimidin-6-yl]phenoxy} acetamide

The compound of this invention was synthesized from the title compound of Preparation 8 and cyclopentylamine following the general procedure described for examples 55-76.

m.p.(MeOH/H_2O): 234-236°C

δ (DMSO): 7.83 (d, 2H), 6.99 (d, 2H), 6.56 (s, 1H), 4.48 (s, 2H), 4.05 (m, 1H), 3.93 (t, 2H), 3.55 (m, 2H), 3.39 (s, 3H), 3.37 (s, 3H), 1.92-1.07 (m, 10H).

EXAMPLE 118

2-{4-[1-(3-Methoxypropyl)-3-methyl-2,4-dioxo-2,3,4,5-tetrahydro-1_H_-pyrrolo[3,2-_d_]pyrimidin-6-yl]phenoxy}-_N_-phenylacetamide

The compound of this invention was synthesized from the title compound of

Preparation 8 and aniline following the general procedure described for examples 55-76.

m.p.(MeOH/H_2O): >251°C (dec.)

δ ^1H NMR ($CDCl_3$): 7.71 (d, 2H), 7.60 (d, 2H), 7.38 (m, 3H), 7.15 (m, 2H), 6.34 (s, 1H), 4.70 (s, 2H), 4.10 (m, 2H), 3.48 (m, 2H), 3.43 (s, 3H), 3.37 (s, 3H), 2.05 (m, 2H).

ESI/MS (m/e,%): 462 (M^+, 100).

EXAMPLES 119-120

The compounds of this invention were synthesized from the title compound of Preparation 9 following the procedure of example 5 and using the corresponding reactant respectively. The ESI/MS data, HPLC retention times and yields are summarised in the following table.

TABLE 20

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
119	$C_{25}H_{26}N_4O_4$	447	9.9	51
120	$C_{29}H_{33}N_5O_4$	516	10.2	64

EXAMPLES 121-123

The compounds of this invention were synthesized from the title compound of Preparation 10 following the procedure of example 5 and using the corresponding reactant respectively. The ESI/MS data, HPLC retention times and yields are summarised in the following table.

TABLE 21

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
121	$C_{26}H_{26}N_4O_6$	491	9.7	57
122	$C_{29}H_{32}N_4O_5$	517	9.8	40
123	$C_{28}H_{31}N_5O_5$	518	9.1	48

EXAMPLE 124

_N_-(4-Bromophenyl)-2-[4-(2,4-dioxo-1-propyl-2,3,4,5-tetrahydro-1_H_-pyrrolo[3,2-_d_]pyrimidin-6-yl)phenoxy] acetamide

Obtained as a white solid (11%) from the title compound of Preparation 10 and 4-bromoaniline following the procedure of Example 4.

m.p.: 276-278 (dec.)

δ ^{1}H NMR (DMSO): 12.00 (bs, 1H), 10.60 (bs, 1H), 10.22 (bs, 1H), 7.86 (d, 2H), 7.60 (d, 2H), 7.40 (d, 2H), 7.09 (d, 2H), 6.60 (s, 1H), 4.78 (s, 2H), 3.80 (t, 2H), 1.64 (m, 2H), 0.90 (t, 3H).

EXAMPLE 125

2-[4-(2,4-Dioxo-1-propyl-2,3,4,5-tetrahydro-1_H_-pyrrolo[3,2-_d_]pyrimidin-6-yl)phenoxy]-_N_-(4-fluorophenyl)acetamide

Obtained as a white solid (56%) from the title compound of Preparation 10 and 4-fluoroaniline following the procedure of Example 4.

m.p.: 306-308°C (dec.)

δ ^{1}H NMR (DMSO): 12.20 (bs, 1H), 10.78 (bs, 1H), 10.15 (bs, 1H), 7.85 (d, 2H), 7.65 (dd, 2H), 7.16 (t, 2H), 7.05 (d, 2H), 6.61 (s, 1H), 4.73 (s, 2H), 3.78 (t, 2H), 1.64 (m, 2H), 0.90 (t, 3H).

EXAMPLE 126-130

The compounds of this invention were synthesized from the title compound of Preparation 11 following the procedure of example 5 and using the corresponding reactant respectively. The ESI/MS data, HPLC retention times and yields are summarised in the following table.

TABLE 22

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
126	$C_{26}H_{28}N_4O_6$	493	9	90
127	$C_{26}H_{27}FN_4O_6$	511	9.1	85
128	$C_{26}H_{27}BrN_4O_6$	573	9.9	84
129	$C_{30}H_{35}N_5O_6$	562	9.4	82
130	$C_{29}H_{32}N_4O_6$	533	9.3	94

EXAMPLES 131-135

The compounds of this invention were synthesized from the title compound of Preparation 12 following the procedure of example 5 and using the corresponding reactant respectively. The ESI/MS data, HPLC retention times and yields are summarised in the following table.

TABLE 23

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
131	$C_{28}H_{28}N_4O_4$	485	10.6	88
132	$C_{28}H_{27}FN_4O_4$	503	10.6	79
133	$C_{28}H_{27}BrN_4O_4$	564	11.2	68

134	$C_{32}H_{35}N_5O_4$	554	10.8	92
135	$C_{31}H_{32}N_4O_4$	525	10.8	95

EXAMPLE 136

2-[4-(7-Chloro-1,3-dimethyl-2,4-dioxo-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)phenoxy]-*N*-(4-cyanophenyl) acetamide

Obtained as a white solid (42%) from the title compound of Preparation 13 and 4-aminobenzonitrile following the procedure of example 5.

ESI/MS m/e: 463 ($[M+H]^+$, $C_{23}H_{18}ClN_5O_4$).

Retention Time (min.): 16.7

EXAMPLES 137-138

The compounds of this invention were synthesized from the title compound of Preparation 14 following the procedure of example 5 and using the corresponding reactant respectively. The ESI/MS data, HPLC retention times and yields are summarised in the following table.

TABLE 24

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
137	$C_{26}H_{27}BrN_4O_4$	540	20.1	55
138	$C_{26}H_{26}BrFN_4O_4$	558	20.1	62

EXAMPLES 139-149

The compounds of this invention were synthesized from the title compound of Preparation 15 following the procedure of example 5 and using the corresponding reactant respectively. The ESI/MS data, HPLC retention times and yields are summarised in the following table.

TABLE 25

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
139	$C_{26}H_{26}ClFN_4O_4$	512	20.0	65
140	$C_{26}H_{27}ClN_4O_4$	494	19.9	72
141	$C_{26}H_{26}BrClN_4O_4$	573	21.0	35
142	$C_{26}H_{26}Cl_2N_4O_4$	529	21.3	74
143	$C_{26}H_{26}Cl_2N_4O_4$	529	20.0	82
144	$C_{26}H_{26}ClFN_4O_4$	512	20.2	78
145	$C_{27}H_{28}ClFN_4O_4$	526	19.7	80
146	$C_{27}H_{29}ClN_4O_5$	525	19.7	48
147	$C_{27}H_{29}ClN_4O_4$	509	19.7	70
148	$C_{27}H_{29}ClN_4O_4$	509	20.5	60
149	$C_{26}H_{26}ClFN_4O_4$	512	20.2	58

EXAMPLES 150-158

The compounds of this invention were synthesized from the title compound of Preparation 16 following the procedure of example 5 and using the corresponding reactant respectively. The ESI/MS data, HPLC retention times and yields are summarised in the following table.

TABLE 26

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
150	$C_{23}H_{22}N_4O_5$	435	10.1	58
151	$C_{23}H_{21}FN_4O_5$	453	10.2	47

152	$C_{24}H_{23}ClN_4O_5$	359	8.4	61
153	$C_{26}H_{26}N_4O_5$	475	10.4	43
154	$C_{27}H_{29}N_5O_5$	504	10.5	60
155	$C_{24}H_{21}N_5O_5$	460	10.0	72
156	$C_{23}H_{21}BrN_4O_5$	513	11.0	70
157	$C_{29}H_{32}N_4O_6$	533	9.8	51
158	$C_{28}H_{31}N_5O_6$	534	9.1	46

EXAMPLES 159-168

The compounds of this invention were synthesized from the title compound of Preparation 17 following the procedure of example 5 and using the corresponding reactant respectively. The ESI/MS data, HPLC retention times and yields are summarised in the following table.

TABLE 27

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
159	$C_{23}H_{22}N_4O_5$	435	10.0	49
160	$C_{23}H_{21}FN_4O_5$	452	10.1	65
161	$C_{24}H_{23}ClN_4O_5$	482	10.3	58
162	$C_{26}H_{26}N_4O_5$	475	10.1	41
163	$C_{27}H_{29}N_5O_5$	504	10.1	45
164	$C_{24}H_{21}N_5O_5$	460	9.8	59
165	$C_{23}H_{21}BrN_4O_5$	514	10.9	70
166	$C_{26}H_{26}N_4O_7$	507	9.6	44
167	$C_{29}H_{32}N_4O_6$	533	9.5	50

168	$C_{28}H_{31}N_5O_6$	534	8.8	39

EXAMPLES 169-174

The compounds of this invention were synthesized from the title compound of Preparation 18 following the procedure of example 5 and using the corresponding reactant respectively. The ESI/MS data, HPLC retention times and yields are summarised in the following table.

TABLE 28

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
169	$C_{27}H_{30}N_4O_4$	475	11.6	59
170	$C_{30}H_{34}N_4O_4$	515	11.9	34
171	$C_{31}H_{37}N_5O_4$	544	11.9	39
172	$C_{28}H_{31}ClN_4O_4$	523	11.9	47
173	$C_{27}H_{29}FN_4O_4$	493	11.7	59
174	$C_{28}H_{32}N_4O_5$	505	11.5	52

EXAMPLES 175-179

The compounds of this invention were synthesized from the title compound of Preparation 19 following the procedure of example 5 and using the corresponding reactant respectively. The ESI/MS data, HPLC retention times and yields are summarised in the following table.

TABLE 29

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
175	$C_{23}H_{22}N_4O_4$	419	8.8	85
176	$C_{23}H_{21}FN_4O_4$	437	9	90
177	$C_{23}H_{21}BrN_4O_4$	498	9.8	55
178	$C_{27}H_{29}N_5O_4$	488	9.3	59
179	$C_{26}H_{26}N_4O_4$	459	9.2	75

EXAMPLES 180-184

The compounds of this invention were synthesized from the title compound of Preparation 20 following the procedure of example 5 and using the corresponding reactant respectively. The ESI/MS data, HPLC retention times and yields are summarised in the following table.

TABLE 30

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
180	$C_{28}H_{32}N_4O_4$	489	10.8	78
181	$C_{28}H_{31}FN_4O_4$	507	10.9	77
182	$C_{28}H_{31}BrN_4O_4$	569	11.4	65
183	$C_{32}H_{39}N_5O_4$	558	11.1	85
184	$C_{31}H_{36}N_4O_4$	529	11.1	82

EXAMPLES 185-189

The compounds of this invention were synthesized from the title compound of

Preparation 21 following the procedure of example 5 and using the corresponding reactant respectively. The ESI/MS data, HPLC retention times and yields are summarised in the following table.

TABLE 31

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
185	$C_{28}H_{32}N_4O_4$	489	10.9	47
186	$C_{28}H_{31}FN_4O_4$	506	10.9	50
187	$C_{28}H_{31}BrN_4O_4$	568	11.5	48
188	$C_{32}H_{39}N_5O_4$	558	11.4	37
189	$C_{31}H_{36}N_4O_4$	529	11.5	30

EXAMPLES 190-192

The compounds of this invention were synthesized from the title compound of Preparation 22 following the procedure of example 5 and using the corresponding reactant respectively. The ESI/MS data, HPLC retention times and yields are summarised in the following table.

TABLE 32

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
190	$C_{32}H_{32}N_4O_4$	537	11.0	93
191	$C_{32}H_{31}FN_4O_4$	555	11.0	20
192	$C_{36}H_{39}N_5O_4$	606	11.4	80

EXAMPLES 193-196

The compounds of this invention were synthesized from the title compound of Preparation 23 following the procedure of example 5 and using the corresponding reactant respectively. The ESI/MS data, HPLC retention times and yields are summarised in the following table.

TABLE 33

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
193	$C_{27}H_{30}N_4O_3$	459	10.3	59
194	$C_{27}H_{29}FN_4O_3$	477	10.4	52
195	$C_{31}H_{37}N_5O_3$	528	10.7	35
196	$C_{30}H_{34}N_4O_3$	499	10.9	21

EXAMPLES 197-199

The compounds of this invention were synthesized from the title compound of Preparation 24 following the procedure of example 5 and using the corresponding reactant respectively. The ESI/MS data, HPLC retention times and yields are summarised in the following table.

TABLE 34

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
197	$C_{27}H_{28}N_4O_3$	457	11.9	66
198	$C_{31}H_{35}N_5O_3$	526	12.2	52
199	$C_{30}H_{32}N_4O_3$	497	12.3	60

EXAMPLES 200-204

The compounds of this invention were synthesized from the title compound of Preparation 25 following the procedure of example 5 and using the corresponding reactant respectively. The ESI/MS data, HPLC retention times and yields are summarised in the following table.

TABLE 35

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
200	$C_{28}H_{32}N_4O_4$	489	10.6	62
201	$C_{28}H_{31}FN_4O_4$	507	10.6	72
202	$C_{32}H_{39}N_5O_4$	558	11.0	48
203	$C_{31}H_{36}N_4O_4$	529	11.1	69
204	$C_{34}H_{41}N_5O_4$	584	11.3	62

EXAMPLES 205-209

The compounds of this invention were synthesized from the title compound of Preparation 26 following the procedure of example 5 and using the corresponding reactant respectively. The ESI/MS data, HPLC retention times and yields are summarised in the following table.

TABLE 36

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
205	$C_{25}H_{26}N_4O_3$	431	10.3	61
206	$C_{25}H_{25}FN_4O_3$	449	10.4	53
207	$C_{25}H_{25}BrN_4O_3$	510	11.1	55

208	$C_{29}H_{33}N_5O_3$	500	10.7	54
209	$C_{28}H_{30}N_4O_3$	471	10.7	48

EXAMPLE 210

6-[4-(3-Phenyl[1,2,4]oxadiazol-5-ylmethoxy)phenyl]-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

a) To a mixture of the title compound of Preparation 2 (400 mg, 1.03 mmol), *N*-(3-dimethylaminopropyl)-*N'*-ethyl-carbodiimide hydrochloride (237 mg, 1.24 mmol) and 1-hydroxybenzotriazole (167 mg, 1.24 mmol) in dimethylformamide (15 mL) was added triethylamine (288 µL, 2.06 mmol) and *N*-hydroxybenzamidine (168 mg, 1.24 mmol). The mixture was stirred at room temperature overnight.

The solvent was evaporated under reduced pressure and the residue was partitioned between dichloromethane and a 1 M aqueous solution of citric acid. The organic phase was separated, washed with a saturated aqueous solution of sodium bicarbonate, dried (Na_2SO_4) and evaporated under reduced pressure. The residue was triturated with ethyl ether and the precipitate was collected by filtration to yield the title compound as a yellow solid (144 mg, 28%).

b) A stirred solution of the above compound (140 mg, 0.277 mmol) in toluene (50 mL) was refluxed using a Dean-Stark apparatus for 20 hours. The solvent was evaporated under reduced pressure, the residue was triturated with ethyl ether and the precipitate was collected by filtration to yield the title compound as a yellow solid (90 mg, 67%).

δ ^{1}H NMR ($CDCl_3$): 10.3 (bs, 1H), 8.1 (m, 2H), 7.7 (d, 2H), 7.5 (d, 2H), 7.2 (d, 1H), 7.1 (d, 1H), 6.2 (s, 1H), 5.4 (s, 2H), 4.0 (m, 4H), 1.7 (m, 4H), 0.9 (dt, 6H).

ESI/MS (m/e,%): 486 (M^+, 100).

Retention Time (min.): 11.4

EXAMPLE 211

6-{4-[2-oxo-2-{[amino(4-fluorophenyl)methylenediamino]-oxy}ethoxy]phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

Obtained as a white solid (88%) from the title compound of Preparation 2 and 4-fluoro-*N*-hydroxybenzamidine following the procedure a) of Example 210.

δ ^{1}H NMR (DMSO): 12.2 (s, 1H), 7.8 (dd, 4H), 7.3 (m, 2H), 7.0 (d, 4H), 6.6 (s, 1H), 5.0 (s, 2H), 3.8 (m, 4H), 1.6 (m, 4H), 0.9 (m, 6H).

ESI/MS (m/e,%): 522 (M^+, 100).

Retention Time (min.): 10.1

EXAMPLE 212

6-{4-[3-(4-Fluorophenyl)[1,2,4]oxadiazol-5-ylmethoxy] phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

Obtained as a white solid (83%) from the title compound of Example 211 following the procedure b) of Example 210.

δ ^{1}H NMR (DMSO): 12.2 (s, 1H), 8.1 (dd, 2H), 7.9 (d, 2H), 7.4 (t, 2H), 7.1 (d, 2H), 6.7 (s, 1H), 5.6 (s, 2H), 3.8 (m, 4H), 1.6 (m, 4H), 0.9 (dt, 6H).

ESI/MS (m/e,%): 504 (M^+, 100).

Retention Time (min.): 11.4

EXAMPLE 213

1,3-Dipropyl-6-[4-(3-pyridin-4-yl[1,2,4]oxadiazol-5-ylmethoxy)phenyl]-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

Obtained as a white solid (87%) from the title compound of Preparation 2 and *N*-hydroxyisonicotinamidine following the same procedure of Example 210.

δ ^{1}H NMR (DMSO): 12.2 (bs, 1H), 8.8 (d, 1H), 8.7 (d, 1H), 7.9 (m, 3H), 7.7 (d, 1H), 7.2 (d, 1H), 7.1 (d, 1H), 6.7 (s, 1H), 5.7 (s, 2H), 3.9 (m, 4H), 1.6 (m, 4H), 0.9 (dt, 6H).

ESI/MS (m/e,%): 487 (M^+, 100).

Retention Time (min.): 10.4

EXAMPLE 214

6-[4-(Benzooxazol-2-ylmethoxy)phenyl]-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione

A stirred solution of the title compound of Example 51 (134 mg, 0.28 ,mmol) and *p*-toluensulfonic acid (48 mg, 0.28 mmol) in toluene (10 mL) was refluxed using a Dean-Stark apparatus for 5 hours. The solvent was evaporated under reduced pressure, the residue was partitioned between dichlorometane and a saturated aqueous solution of sodium bicarbonate. The organic phase was separated, washed with brine, dried ($MgSO_4$) and evaporated under reduced pressure. The residue was triturated with ethyl ether and the precipitate was collected by filtration to yield the title compound as a white solid (82 mg, 64%).

δ ^{1}H NMR ($CDCl_3$): 10.9 (s, 1H), 7.7 (m, 3H), 7.5 (m, 1H), 7.3 (dd, 2H), 7.1 (d, 2H), 6.1 (s, 1H), 5.3 (s, 2H), 3.9 (m, 4H), 1.7 (dq, 4H), 0.9 (dt, 6H).

ESI/MS (m/e,%): 459 (M^+, 100).

Retention Time (min.): 10.9

EXAMPLE 215

6-[4-(5-Phenyl-4,5-dihydrooxazol-2-ylmethoxy)phenyl]-1,3-dipropyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

A solution of the title compound of Example 43 (60 mg, 0.119 mmol) in thionyl chloride (173 μL) was stirred at room temperature for 1 hour. The resulting solution was poured into water and a yellow solid precipitated. A suspension of the above solid in water was treated with a 2 N aqueous solution of sodium hydroxide until alkaline pH. The solid was collected by filtration and dried to yield the title compund as a yellow solid (35 mg, 60%).

ESI/MS (m/e,%): 487 (M^+, 100).

Retention Time (min.): 10.7

EXAMPLE 216

6-[4-(4-Methyl-5-phenyl-4,5-dihydrooxazol-2-ylmethoxy)-phenyl]-1,3-dipropyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

Obtained as a yellow solid (45%) from the title compound of Example 44 following procedure of Example 215.

ESI/MS (m/e,%): 501 (M^+, 100).

Retention Time (min.): 11.0

EXAMPLE 217

6-[4-(7-Benzyl-1-oxa-3,7-diazaspiro[4.5]dec-2-en-2-ylmethoxy)phenyl]-1,3-dipropyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

Obtained as a white solid (33%) from the title compound of Example 46 following the procedure described in Example 215.

ESI/MS (m/e,%): 570 (M^+, 100).

Retention Time (min.): 7.3

EXAMPLE 218

1,3-Dipropyl-6-[4-(quinolin-2-ylmethoxy)phenyl]-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

a) A mixture of *p*-hydroxybenzaldehyde (17.02 g, 0.139 mmol), 2-chloromethylquinoline (24.76 g, 0.139 mmol), potassium carbonate (57.64 g, 0.417 mmol) and potassium iodide (2.17 g, 0.013 mmol) in methyl isobutyl ketone (515 mL) was refluxed for 20 h. After cooling to room temperature, the inorganic salts were filtered and the solvent was evaporated under reduced pressure. The residue was partitioned between dichlorometane and water, the aqueous phase extracted with dichloromethane and the organic phase washed with water and brine, dried ($MgSO_4$) and evaporated under reduced pressure. The residue was triturated with ethyl ether and the precipitate was collected by filtration to yield the 4-(quinolin-2-

ylmethoxy)benzaldehyde as a yellow solid (25.62 g, 70%).

m.p.: 70.0-72.0°C

b) The title compound was obtained as a yellow solid (560 mg, 61%) from 6-methyl-5-nitro-1,3-dipropyl-1*H* pyrimidine-2,4-dione (1.0 g, 3.92 mmol) and 4-(quinolin-2-ylmethoxy)benzaldehyde (1.13 g, 4.31 mmol) following the same procedure described in Preparation 2.

δ ^{1}H NMR ($CDCl_3$): 10.5 (s, 1H), 8.3 (d, 2H), 7.7 (m, 6H), 7.1 (d, 2H), 6.2 (s, 1H), 5.5 (s, 2H), 3.9 (m, 4H), 1.7 (m, 4H), 0.9 (dt, 6H).

ESI/MS (m/e,%): 469 (M^+, 100).

Retention Time (min.): 11.3

EXAMPLES 219-226

The compounds of this invention were synthesized from the title compound of Preparation 2 following the procedure of example 5 and using the corresponding reactant respectively. The ESI/MS data, HPLC retention times and yields are summarised in the following table.

TABLE 37

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
219	$C_{25}H_{27}N_5O_4$	462	10.1	54
220	$C_{25}H_{27}N_5O_5$	478	9.5	36
221	$C_{26}H_{29}N_5O_4$	476	10.5	26
222	$C_{25}H_{27}N_5O_4$	462	9.3	70
223	$C_{26}H_{29}N_5O_5$	492	10.0	36
224	$C_{26}H_{29}N_5O_4$	476	7.6	40

225	$C_{31}H_{34}F_3N_5O_4$	598	11.0	42
226	$C_{30}H_{34}ClN_5O_4$	566	11.0	60

EXAMPLES 227-229

The compounds of this invention were synthesized from the title compound of Preparation 2 following the procedure of example 5a and using the corresponding reactant respectively. The ESI/MS data and yields are summarised in the following table.

TABLE 38

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Yield %
227	$C_{24}H_{26}N_6O_4$	463	54
228	$C_{26}H_{30}N_6O_6$	523	25
229	$C_{23}H_{26}N_6O_4$	450	37

(Example 227) δ ^{1}H NMR (DMSO): 12.33 (bs, 1H), 11.05 (bs, 1H), 9.41 (s, 1H), 8.52 (m, 2H), 7.97 (d, 2H), 7.14 (d, 2H), 6.76 (s, 1H), 5.01 (s, 2H), 3.95 (m, 4H), 1.70 (m, 4H), 1.00 (m, 6H).

(Example 228) δ ^{1}H NMR (DMSO): 12.43 (bs, 1H), 11.04 (bs, 1H), 8.06 (d, 2H), 7.20 (m, 3H), 6.85 (bs, 1H), 5.08 (s, 2H), 4.08 (m, 10H), 1.80 (m, 4H), 1.07 (m, 6H).

(Example 229) δ ^{1}H NMR (DMSO): 12.27 (bs, 1H), 8.97 (d, 1H), 8.11 (d, 2H), 7.03 (d, 2H), 6.67 (s, 1H), 6.03 (d, 1H), 5.84 (s, 2H), 5.44 (s, 2H), 3.90 (m, 4H), 1.60 (m, 4H), 0.90 (m, 6H).

EXAMPLES 230-239

The compounds of this invention were synthesized from the title compound of Preparation 4 following the procedure of example 5 and using the corresponding reactant respectively. The ESI/MS data, HPLC retention times and yields are summarised in the following table.

TABLE 39

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
230	$C_{26}H_{26}ClN_5O_4$	509	9.8	18
231	$C_{27}H_{26}F_3N_5O_4$	542	10.0	58
232	$C_{26}H_{26}BrN_5O_4$	552	9.9	33
233	$C_{27}H_{28}N_4O_5$	489	8.4	40
234	$C_{28}H_{27}N_5O_4$	498	9.1	17
235	$C_{33}H_{32}N_4O_4$	549	10.4	27
236	$C_{27}H_{27}ClN_4O_5$	524	9.1	45
237	$C_{25}H_{24}Cl_2N_6O_4$	543	9.2	68
238	$C_{27}H_{25}ClN_6O_4S$	566	10.1	52
239	$C_{27}H_{25}N_5O_4$	484	9.4	63

EXAMPLES 240-242

The compounds of this invention were synthesized from the title compound of Preparation 3 following the procedure of example 55 and using the corresponding reactant respectively. The ESI/MS data, HPLC retention times and yields are

summarised in the following table.

TABLE 40

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Yield %
240	$C_{28}H_{27}FN_4O_5$	519	40
241	$C_{22}H_{21}N_5O_4$	419	71
242	$C_{23}H_{27}N_5O_6$	469	42

(Example 240) δ ^{1}H NMR (DMSO): 12.29 (bs, 1H), 8.13 (dd, 2H), 7.85 (d, 2H), 7.40 (m, 2H), 7.00 (d, 2H), 6.65 (s, 1H), 4.92 (d, 2H), 4.37 (d, 1H), 3.92 (d, 1H), 3.76 (m, 1H), 3.47 (m, 1H), 3.43 (s, 3H), 3.27 (s, 3H), 2.82 (m, 1H), 1.84 (m, 2H), 1.61 (m, 1H), 1.41 (m, 1H).

(Example 241) δ ^{1}H NMR (DMSO): 12.30 (bs, 1H), 8.79 (m, 1H), 8.50 (m, 1H), 7.89 (d, 2H), 7.25 (d, 2H), 7.01 (d, 2H), 6.66 (d, 1H), 4.68 (s, 2H), 4.38 (d, 2H), 3.43 (s, 3H), 3.27 (s, 3H).

(Example 242) δ ^{1}H NMR (DMSO): 12.32 (bs, 1H), 7.89 (d, 2H), 7.05 (d, 2H), 6.66 (s, 1H), 4.96 (s, 2H), 4.10 (m, 2H), 3.40 (m, 14H), 1.25 (s, 3H).

EXAMPLES 243-246

The compounds of this invention were synthesized from the title compound of Preparation 6 following the procedure of example 5 and using the corresponding reactant respectively. The ESI/MS data, HPLC retention times and yields are summarised in the following table.

TABLE 41

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
243	$C_{30}H_{34}N_4O_5$	531	10.3	70
244	$C_{27}H_{28}Cl_2N_6O_4$	571	9.8	40
245	$C_{24}H_{25}N_5O_5$	463	8.9	65
246	$C_{29}H_{30}F_3N_5O_4$	570	10.4	26

EXAMPLES 247-253

The compounds of this invention were synthesized from the title compound of Preparation X following the procedure of example 5 and using the corresponding reactant respectively. The ESI/MS data, HPLC retention times and yields are summarised in the following table.

TABLE 42

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
247	$C_{21}H_{24}N_4O_5$	412	6.6	50
248	$C_{22}H_{27}N_5O_4$	425	4.7	41
249	$C_{19}H_{22}N_4O_5$	386	6.1	36
250	$C_{28}H_{31}N_5O_5$	518	8.4	29
251	$C_{28}H_{31}N_5O_4$	502	5.7	44

(Example 252) δ ^{1}H NMR (DMSO): 12.15 (bs, 1H), 11.18 (bs, 1H), 10.27 (bs, 1H), 7.91 (d, 2H), 7.76 (m, 2H), 7.54 (m, 4H), 6.29 (s, 1H), 4.83 (s, 2H), 3.91 (m, 2H), 1.66 (m, 2H), 0.95 (t, 3H).

(Example 253) δ ^{1}H NMR (DMSO): 12.03 (bs, 1H), 11.20 (bs, 1H), 10.25 (bs, 1H), 7.81 (d, 2H), 7.61 (d, 2H), 7.50 (d, 2H), 7.02 (d, 2H), 6.19 (s, 1H), 4.74 (s, 2H), 3.80 (m, 2H), 1.55 (m, 2H), 0.86 (t, 3H).

EXAMPLE 254

6-{4-[2-Oxo-2-(4-phenylpiperazin-1-yl)-ethoxy]phenyl}-1-propyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

Obtained as a white solid (2%) from the title compound of Preparation 10 and 1-phenyl piperazine following the procedure of example 5.

m.p.(MeOH/H_2O): 280-282°C

δ ^{1}H NMR (DMSO): 12.19 (s, 1H), 10.78 (s, 1H), 7.81 (d, 2H), 7.22 (m, 2H), 6.96 (m, 4H), 6.80 (t, 1H), 6.60 (s, 1H), 4.92 (s, 2H), 3.78 (m, 2H), 3.60 (m, 4H), 3.15 (m, 4H), 1.66 (m, 2H), 0.90 (t, 3H).

ESI/MS (m/e,%): 487 (M^+, 33).

EXAMPLES 255-257

The compounds of this invention were synthesized from the title compound of Preparation 28 following the procedure of example 5 and using the corresponding reactant respectively. The ESI/MS data, HPLC retention times and yields are summarised in the following table.

TABLE 43

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
255	$C_{32}H_{37}FN_6O_5$	605	9.8	80
256	$C_{32}H_{38}N_6O_5$	587	6.5	61
257	$C_{33}H_{37}F_3N_6O_5$	655	7.5	39

EXAMPLE 258

Pyrazin-2-yl-carbamic acid 4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimid in-6-yl)benzyl ester

a)To a solution of triphosgene (87 mg, 0.29 mmol) in anhydrous dioxane (5 mL) under argon atmosphere was slowly added at room temperature a solution of 2-aminopyrazine (84 mg, 0.89 mmol) and triethylamine (0.24 mL, 1.76 mmol) in dioxane (5 mL). The mixture was stirred at room temperature for 1 hour.

b)Then the title compound of Preparation 30 was added to the above reaction mixture (100 mg, 0.29 mmol) and the solution was stirred 48 hours at room temperature. The mixture was evaporated under reduced pressure and the residue was partitioned between dichloromethane and a saturated aqueous solution of sodium bicarbonate. The organic phase was separated, washed with water and brine, dried (Na_2SO_4) and evaporated under reduced pressure. The resulting crude was purified by flash column chromatography on silica-gel (dichloromethane/MeOH 95:5) to yield the title compound as a white solid (25 mg, 19%).

m.p.(MeOH): 267-270°C

δ ^{1}H NMR (DMSO): 12.56 (s, 1H), 10.83 (s, 1H), 9.27 (s, 1H), 8.50 (m, 2H), 8.11 (d, 2H), 7.66 (d, 2H), 6.95 (s, 1H), 5.40 (s, 2H), 4.02 (m, 4H), 1.75 (m, 4H), 1.05

(m, 6H).

EXAMPLE 259

(2,6-Dimethoxy-pyrimidin-4-yl)-carbamic acid 4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)benzyl ester

Obtained as a white solid (20%) from the title compound of Preparation 30 and 4-amino-2,6-dimethoxypyrimidine following the procedure of example 258.

m.p.(MeOH): 182-185°C

δ ^{1}H NMR (DMSO): 12.5 (bs, 1H), 10.73 (s, 1H), 8.04 (d, 2H), 7.57 (d, 2H), 6.94 (s, 1H), 6.89 (s, 1H), 5.30 (s, 2H), 3.96 (m, 4H), 1.73 (m, 4H), 0.98 (m, 6H).

ESI/MS (m/e,%): 523; 342 (100).

EXAMPLE 260

Pyridin-4-ylmethyl carbamic acid 4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]p
yrimidin-6-yl)benzyl ester

To a solution of 1,1'-carbonyldiimidazole (48 mg, 0.29 mmol) in pyridine (0.5 mL) under argon atmosphere was slowly added at 0°C a solution of the title compound of Preparation 30 (100 mg, 0.29 mmol) in pyridine (1 mL). The mixture was stirred at room temperature for for 1 hour. Then the title compound of Preparation 30 was added (100 mg, 0.29 mmol) and the mixture was stirred 2 hours at 0°C and 2 hours at room temperature. To the reaction mixture was slowly added 1-phenylpyperacine (162 mg, 0.29 mmol) and the mixture was stirred at room temperature overnight. The resulting solution was cooled to 4°C and the precipitate was collected by filtration to yield the title compound as a white solid (51 mg, 33%).

m.p.(MeOH): 240-242°C

δ ^{1}H NMR (DMSO): 12.36 (bs, 1H), 7.90 (d, 2H), 7.42 (d, 2H), 7.03 (m, 2H), 6.95 (m,

2H), 6.73 (s, 1H), 5.11 (s, 2H), 3.85 (m, 4H), 3.53 (m, 4H), 3.04 (m, 4H), 1.67 (m, 2H), 1.56 (m, 2H), 0.88 (m, 6H).

EXAMPLE 261

4-(3-Chlorophenyl)piperazine-1-carboxylic acid 4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)benzyl ester

Obtained as a white solid (15%) from the title compound of Preparation 30 and 1-(3-Chloro phenyl) piperazine following the procedure of example 260.

m.p.(MeOH): 188-190°C

δ ^{1}H NMR (DMSO): 12.36 (s, 1H), 7.91 (d, 2H), 7.42 (d, 2H), 7.21 (m, 1H), 6.88 (m, 2H), 6.74 (m, 2H), 5.11 (s, 2H), 3.86 (m, 4H), 3.18 (m, 4H), 1.40 (m, 4H), 0.88 (m, 6H).

ESI/MS (m/e,%): 476; 324 (100).

EXAMPLE 262

(1H-Pyrazol-3-yl)carbamic acid 4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]
pyrimidin-6-yl)benzyl ester

Obtained as a white solid (60%) from the title compound of Preparation 30 and 1*H*-pyrazol-3-ylamine following the procedure of example 260.

m.p.(MeOH): 210-213°C

δ ^{1}H NMR (DMSO): 12.39 (bs, 1H), 7.93 (m, 4H), 7.49 (d, 2H), 6.76 (s, 1H), 5.85 (s, 1H), 5.51 (s, 1H), 5.33 (s, 2H), 3.86 (m, 4H), 1.75 (m, 4H), 0.88 (m, 6H).

EXAMPLE 263

4-(3-Trifluoromethylphenyl)piperazine-1-carboxylic acid 4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)benzyl ester

Obtained as a white solid (42%) from the title compound of Preparation 30 and 1-(3-trifluoro methylphenyl)piperazine following the procedure of example 260.

m.p.(MeOH): 232-233°C

δ ^{1}H NMR (DMSO): 12.38 (s, 1H), 7.91 (m, 2H), 7.43 (m, 3H), 7.20 (m, 2H), 7.08 (m, 1H), 6.75 (s, 1H), 5.11 (s, 2H), 3.86 (m, 4H), 3.55 (m, 4H), 3.23 (m, 4H), 1.60 (m, 4H), 0.88 (m, 6H).

EXAMPLE 264

Isoxazol-3-yl-carbamic acid 4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimi din-6-yl)benzyl ester

Obtained as a white solid (41%) from the title compound of Preparation 30 and isoxazol-3-ylamine following the procedure of example 260.

m.p.(MeOH): 168-171°C

δ ^{1}H NMR (DMSO): 12.40 (bs, 1H), 8.30 (m, 1H), 7.95 (d, 2H), 7.62 (s, 1H), 7.55 (d, 2H), 7.07 (s, 1H), 6.76 (s, 1H), 5.45 (s, 2H), 3.86 (m, 4H), 1.60 (m, 4H), 0.88 (m, 6H).

EXAMPLE 265-272

The compounds of this invention were synthesized from the title compound of Preparation 29 following the procedure of example 258 and using the corresponding reactant respectively. The ESI/MS data, melting points and yields are summarised in the following table.

TABLE 44

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	m.p. (°C) (MeOH)	Yield %
265	$C_{22}H_{19}FN_4O_4$	423	-	30
266	$C_{23}H_{22}N_4O_4$	419	-	30
267	$C_{22}H_{20}N_4O_4$	405	-	40
268	$C_{21}H_{19}N_5O_4$	406	301	60
269	$C_{22}H_{21}N_5O_4$	420	293	51
270	$C_{20}H_{18}N_4O_4S$	411	287	31
271	$C_{20}H_{18}N_4O_4S$	411	280	20
272	$C_{20}H_{18}N_4O_5$	395	278	23

(Example 265) δ ^{1}H NMR (DMSO): 12.52 (bs, 1H), 9.91 (s, 1H), 8.00 (d, 2H), 7.55 (m, 2H), 7.20 (m, 2H), 6.83 (s, 1H), 5.24 (s, 2H), 3.50 (s, 3H), 3.33 (s, 3H).

(Example 266) δ ^{1}H NMR (DMSO): 12.53 (bs, 1H), 7.91 (d, 2H), 7.41 (d, 2H), 7.30 (m, 5H), 6.75 (s, 1H), 5.07 (s, 2H), 4.21 (d, 2H), 3.42 (s, 3H), 3.26 (s, 3H).

(Example 267) δ ^{1}H NMR (DMSO): 12.50 (bs, 1H), 9.85 (s, 1H), 8.00 (d, 2H), 7.53 (m, 4H), 7.33 (m, 2H), 7.05 (m, 1H), 6.81 (s, 1H), 5.23 (s, 2H), 3.49 (s, 3H), 3.32 (s, 3H).

EXAMPLE 273-274

The compounds of this invention were synthesized from the title compound of Preparation 30 following the procedure of example 260 and using the corresponding reactant respectively. The ESI/MS data and yields are summarised in the following table.

TABLE 45

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Yield %
273	$C_{26}H_{27}N_5O_4$	474	60
274	$C_{25}H_{24}N_4O_4$	445	45

EXAMPLE 275

Thiophen-2-yl-carbamic acid 2-[4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy]ethyl ester

a) From the title compound of Preparation 2 following the procedure of Preparation 29c, 6-[4-(2-hydroxyethoxy)phenyl]-1,3-dipropyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione was obtained (70%) as a white solid.

δ ^{1}H NMR (DMSO): 12.04 (bs, 1H), 7.68 (d, 2H), 6.82 (d, 2H), 6.47 (d, 1H), 4.71 (t, 1H), 3.86 (m, 2H), 3.68 (m, 4H), 3.54 (m, 2H), 1.45 (m, 4H), 0.72 (m, 6H).

b) The title compound was obtained as a white solid (60%) from the above compound and 2-isocyanatothiophene following the procedure of example 258.

m.p.(MeOH/Et_2O): 223-225°C

δ ^{1}H NMR (DMSO): 12.29 (bs, 1H), 10.86 (bs, 1H), 7.94 (d, 2H), 7.10 (d, 2H), 6.99 (dd, 1H), 6.87 (dd, 1H), 6.73 (s, 1H), 6.63 (dd, 1H), 4.52 (m, 2H), 4.35 (m, 2H), 3.93 (m, 4H), 1.69 (m, 4H), 0.95 (m, 6H).

EXAMPLE 276

(4-Bromophenyl)-carbamic acid 2-[4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)phenoxy]ethyl ester

Obtained as a brownish solid (23%) from the title compound of Preparation 2 and 4-bromo phenylisocyanate following the procedure of example 275.

m.p.(MeOH): 281°C (dec.)

δ ^{1}H NMR (DMSO): 12.23 (bs, 1H), 9.99 (s, 1H), 7.88 (d, 2H), 7.46 (m, 4H), 7.04 (d, 2H), 6.66 (s, 1H), 4.44 (m, 2H), 4.30 (m, 2H), 3.86 (m, 4H), 1.62 (m, 4H), 0.90 (m, 6H).

EXAMPLE 277

1-[1-(2,6-Difluoro-phenyl)methanoyl]-3-[4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1H-pyrrolo[3,2-d]pyrimidin-6-yl)benzyl]urea

a) To a suspension of the title compound of Preparation 30 (0.48 g, 1.40 mmol) in dichloromethane (45 mL) was added methanesulfonyl chloride (545 µL, 7.04 mmol) and triethyl amine (981 µL, 7.04 mmol) and the mixture was stirred at room temperature for 5 hours. The solvent was evaporated under reduced pressure, the residue was triturated with dichloromethane and the resulting solid was filtered, washed with dichloromethane and dried to yield methanesulfonic acid 4-(2,4-dioxo-1,3-dipropyl-2,3,4,5-tetrahydro-1*H*-pyrrolo[3,2-*d*]pyrimidin-6-yl)benzyl ester (0.22 g, 37%) as a yellow solid.

b) To a suspension of the above compound (0.22g, 0.52 mmol) in dimethylformamide (5.5 mL) under argon atmosphere, was added sodium azide (68 mg, 1.05 mmol) and the mixture was heated at 40 °C for 4 hours. The solvent was evaporated under reduced pressure, the residue was triturated with water and the resulting solid was filtrated, washed with water and diethyl ether and dried to yield 6-(4-azidomethylphenyl)-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione (0.15 g, 79%) as a yellow solid.

c) To a suspension of the above compound (0.15 g, 0.41 mmol) in tetrahydrofuran (2 mL) at 0 °C, was added a solution of 1 M trimethyl phosphine in toluene (656 µL, 0.65 mmol) and the resulting solution was stirred at room temperature for 5 hours. Water (22 µL, 1.23 mmol) was added and the solution was stirred at room temperature for 18 hours. The solvent was evaporated under reduced pressure, the residue was triturated with dichloromethane and the resulting solid was filtrated, washed

with dichloromethane and dried to yield 6-(4-aminomethylphenyl)-1,3-dipropyl-1,5-dihydropyrrolo[3,2-*d*]pyrimidine-2,4-dione (96 mg, 69%) as a yellow solid.

d) To a solution of the above compound (25 mg, 0.07 mmol) in dimethylformamide (1 mL) was added 2,6-difluorobenzoyl isocyanate (20 mg, 0.088 mmol) and the mixture was stirred at room temperature for 4 hours. Tris-(2-aminoethyl)amine polystyrene (0.12 g, 0.44 mmol) was added and the mixture was stirred for 1 hour. After filtration, the solvent was evaporated under reduced pressure, the residue was triturated with a mixture of diethyl ether and dichloromethane and the resulting solid was filtrated, washed with diethyl ether and dried to yield the title compound (53%) as a yellow solid.

ESI/MS m/e: 524 ($[M+H]^+$, $C_{27}H_{27}F_2N_5O_4$).

Retention Time (min.): 10.1

EXAMPLE 278-279

The compounds of this invention were synthesized from the title compound of Preparation 2 following the procedure of example 214 and using the corresponding reactant respectively. The ESI/MS data, HPLC retention times and yields are summarised in the following table.

TABLE 46

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
278	$C_{26}H_{25}FN_4O_4$	477	11.0	63
279	$C_{26}H_{27}N_5O_3$	458	9.6	67

EXAMPLE 280

1,3-Dimethyl-6-[4-(quinolin-2-ylmethoxy)phenyl]-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

Obtained as a white solid (50%) from 6-methyl-5-nitro-1,3-dimethyl-1*H*-pyrimidine-2,4-dione and 4-(quinolin-2-ylmethoxy)benzaldehyde following the procedure of example 218.

ESI/MS m/e: 413 ($[M+H]^+$, $C_{24}H_{20}N_4O_3$).

Retention Time (min.): 9.7

EXAMPLE 281

1,3-Dimethyl-6-[4-(3-phenyl[1,2,4]oxadiazol-5-ylmethoxy)phenyl]-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

Obtained as a white solid (60%) from the title compound of Preparation 4 and *N*-hydroxybenzamidine following the procedure of example 210.

ESI/MS m/e: 430 ($[M+H]^+$, $C_{23}H_{19}N_5O_4$).

Retention Time (min.): 10.0

EXAMPLE 282-284

The compounds of this invention were synthesized from the title compound of Preparation 6 following the procedure of example 210 and using the corresponding reactant respectively. The ESI/MS data, HPLC retention times and yields are summarised in the following table.

TABLE 47

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
282	$C_{25}H_{23}N_5O_4$	458	10.7	54

283	$C_{25}H_{22}FN_5O_4$	476	10.9	43
284	$C_{24}H_{21}ClN_4O_4$	465	10.8	60

EXAMPLE 285

6-{4-[3-(4-Bromophenyl)[1,2,4]oxadiazol-5-ylmethoxy]-phenyl}-3-propyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

Obtained as a white solid (30%) from the title compound of Preparation 27 and 4-bromo-*N*-hydroxybenzamidine following the procedure of example 210.

δ ^{1}H NMR (DMSO): 12.13 (bs, 1H), 11.16 (bs, 1H), 7.96 (d, 2H), 7.85 (d, 4H), 7.15 (d, 2H), 6.24 (s, 1H), 5.67 (s, 2H), 3.83 (m, 2H), 1.58 (m, 2H), 0.88 (m, 3H).

EXAMPLE 286-289

The compounds of this invention were synthesized from the title compound of Preparation 19 following the procedure of example 210 and using the corresponding reactant respectively. The ESI/MS data, HPLC retention times and yields are summarised in the following table.

TABLE 48

Example	Molecular Formula	ESI/MS m/e $[M+H]^+$	Retention Time (min.)	Yield %
286	$C_{24}H_{21}N_5O_4$	444	10.4	44
287	$C_{24}H_{20}FN_5O_4$	462	10.5	26
288	$C_{22}H_{19}N_5O_4S$	450	10.0	55
289	$C_{25}H_{23}N_5O_4S$	490	10.9	58

EXAMPLE 290

6-{4-[(4-Bromophenylamino)methyl]phenyl}-1,3-dipropyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione

a) To a solution of the title compound of Preparation 30 (200mg, 0.59 mmol) in DMF (5 mL) was added CBr_4 (480 mg, 1.02 mmol) and the mixture was cooled to 0°C. Then a solution of triphenyl phosphine (270 mg, 1.02 mmol) in DMF (2 mL) was added and the mixture was stirred at room temperature for 14 hours. The precipitate was collected by filtration and used in the next step without further purification.

b) To a solution of 4-bromoaniline (43 mg, 0.25 mmol) in ethanol (2 mL) was added K_2CO_3 (34 mg, 0.025 mmol) and the above bromide (20 mg, 0.05 mmol). The mixture was refluxed for 1 hour. The solvent was evaporated under reduced pressure, the residue was suspended in chloroform, the organic phase was washed with water, dried (Na_2SO_4) and evaporated. Flash column chromatography (chloroform:petroleum ether 9:1) provided the title compound as a brown solid (11 mg, 44%).

m.p.(MeOH): >250°C

δ ^{1}H NMR (DMSO): 10.7 (bs, 1H), 7.72 (d, 2H), 7.42 (d, 2H), 7.24 (d, 2H), 6.50 (d, 2H), 6.24 (s, 1H), 4.36 (s, 2H), 3.95 (m, 4H), 1.75 (m, 4H), 0.95 (m, 6H).

EXAMPLE 291

6-(4-Phenylaminomethylphenyl)-1,3-dipropyl-1,5-dihydropyrrolo[3,2-d]pyrimidine-2,4-dione.

Obtained as a brownish solid (64%) from the title compound of Preparation 30 and aniline following the procedure of example 290.

m.p.(MeOH): 201°C

δ ^{1}H NMR (DMSO): 10.51 (bs, 1H), 7.70 (m, 1H), 7.46 (m, 1H), 7.24 (m, 4H), 6.75 (m, 3H), 6.24 (s, 1H), 4.39 (s, 2H), 3.96 (m, 4H), 1.70 (m, 4H), 1.00 (m, 6H).

The following examples illustrate pharmaceutical compositions according to the present invention and procedures for their preparation.

COMPOSITION EXAMPLE 1

50,000 capsules each containing 100 mg of active ingredient were prepared according to the following formulation:

Active ingredient	5 Kg
Lactose monohydrate	10 Kg
Colloidal silicone dioxide	0.1 Kg
Corn starch	1 Kg
Magnesium stearate	0.2 Kg

Procedure

The above ingredients were sieved through a 60 mesh sieve, and were loaded into a suitable mixer and filled into 50,000 gelatine capsules.

COMPOSITION EXAMPLE 2

50,000 Tablets each containing 50 mg of active ingredient were prepared from the following formulation:

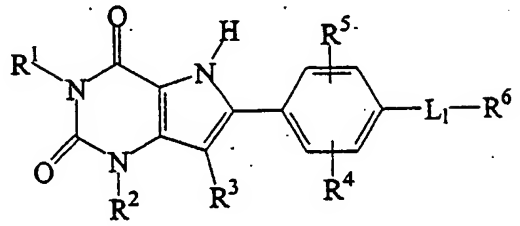
Active ingredient	2.5 Kg
Microcrystalline cellulose	1.95 Kg
Spray dried lactose	9.95 Kg
Carboxymethyl starch	0.4 Kg
Sodium stearyl fumarate	0.1 Kg
Colloidal silicon dioxide	0.1 Kg

Procedure.

All the powders were passed through a screen with an aperture of 0.6 mm, then mixed in a suitable mixer for 20 minutes and compressed into 300 mg tablets using 9 mm disc and flat bevelled punches. The disintegration time of the tablets was about 3 minutes.

CLAIMS

1. A 6-phenylpyrrolopyrimidinedione derivative of the formula (I), or a pharmaceutically acceptable salt thereof,



(I)

wherein:

- R^1 and R^2 are the same or different and each represents hydrogen, a group of formula $-(CH_2)_n-R^7$, or an alkyl group which is unsubstituted or substituted by one or more substituents selected from hydroxy, alkoxy, alkylthio, amino, mono- or di-alkylamino, hydroxycarbonyl, alkoxycarbonyl, acylamino, carbamoyl, alkylcarbamoyl, dihydroxyphosphoryloxy and dialkoxyphosphoryloxy groups,

wherein n is an integer of from 0 to 4 and R^7 represents a cycloalkyl group, a phenyl group or a cyclic group which is a 3- to 7-membered, aromatic or non-aromatic ring, which contains from 1 to 4 heteroatoms selected from N, O and S and which is optionally fused to an aromatic or heteroaromatic ring, the phenyl group being unsubstituted or substituted by one or more substituents selected from halogen, alkyl, aryl, heteroaryl, heterocyclyl, hydroxy, alkylenedioxy, alkoxy, alkylthio, amino, mono- or di-alkylamino, nitro, cyano, hydroxycarbonyl, alkoxycarbonyl, acylamino, carbamoyl, alkylcarbamoyl, dihydrophosphoryloxy, dialkoxyphosphoryloxy and haloalkyl groups and the cyclic group being unsubstituted or substituted by one or more substituents selected from halogen, hydroxy, alkoxy, phenyl, alkoxycarbonyl, amino, mono-alkylamino, di-alkylamino, hydroxycarbonyl, and alkyl groups, the alkyl substituents being unsubstituted or substituted by one or more further substituents selected from halogen, hydroxy, alkoxy, alkylthio, acylamino, carbamoyl,

alkylcarbamoyl, dihydroxyphosphoryloxy, dialkoxyphosphoryloxy, hydroxyalkoxy, phenyl, alkoxycarbonyl, amino, mono- and di-alkylamino and hydroxycarbonyl groups;

- R^3 represents hydrogen, halogen, or a nitro, alkoxycarbonyl or alkyl group, the alkyl group being unsubstituted or substituted by one or more substituents selected from hydroxy, halogen, alkoxy, alkylthio, amino, mono- or di-alkylamino, hydroxycarbonyl, alkoxycarbonyl, acylamino, carbamoyl and alkylcarbamoyl groups;

- R^4 and R^5 are the same or different and each represents hydrogen, halogen, alkyl, hydroxy, alkoxy, alkylthio, dialkylaminoalkoxy, amino, mono- or dialkylamino, nitro, cyano or haloalkyl, or R^4 and R^5, together with the atoms to which they are attached, form a 5 to 7 membered ring containing from 0 to 4 heteroatoms selected from N, O and S;

- L_1 is a direct bond or is -O-, -S-, -N(Z)-, $-O(CH_2)_m-$, $-O(CR^8R^9)_m-$, $-S(CR^8R^9)_m-$, -CH=CH-, $-(CH_2)_m-$, $-(CR^8R^9)_m-$, $-(CH_2)_mO-$, $-(CR^8R^9)_mO-$, $-O(CH_2)_mO-$, $-O(CR^8R^9)_mO-$, $-(CR^8R^9)_m N(Z)-$ or $-N(Z)(CR^8R^9)_m-$ wherein m is an integer of from 1 to 6 and either Z, R^8 and R^9 are the same or different and each represent a group selected from hydrogen, C_1-C_6 alkyl, cycloalkyl, cycloalkyl-C_1-C_6 alkyl, heterocyclyl, heterocyclyl-C_1-C_6 alkyl, aryl, aryl-C_1-C_6 alkyl, heteroaryl, heteroaryl-C_1-C_6 alkyl, hydroxy, C_1-C_6 alkoxy, halogen, cyano, C_1-C_6 alkoxycarbonyl, carbamoyl and haloalkyl, the alkyl, cycloalkyl, heterocyclyl, aryl and heteroaryl moieties being unsubstituted or substituted with one to four substituents independently selected from R^1, or Z is as defined above and R^8 and R^9, together with the atom to which they are attached, form a 4 to 8 membered ring; and

- R^6 represents $-C(O)NR^{10}R^{11}$, $-S(O)_2NR^{10}R^{11}$, $-ON=CR^{12}R^{13}$, or a heterocyclyl, aryl or heteroaryl group, the heterocyclyl, aryl and heteroaryl groups being unsubstituted or substituted with substituents R^{14} to R^{17}, wherein:

R^{10} and R^{11} are either

(a) the same or different, each independently representing hydrogen, an alkyl group, a cycloalkyl group or a phenyl group, wherein (i) the alkyl group is unsubstituted or substituted by one or more substituents selected from hydroxy, halogen, alkoxy,

alkylthio, amino and mono- and di-alkylamino groups, (ii) the cycloalkyl group is optionally fused to an aromatic ring and (iii) the cycloalkyl group and the phenyl group are unsubstituted or substituted by one or more substituents selected from (1) groups of formula $-(CH_2)_n R^7$, $-O-(CH_2)_n R^7$, $-S-(CH_2)_n R^7$, -COR and -CONHR, wherein R is alkyl or $-(CH_2)_n R^7$ and n and R^7 are as defined above, (2) groups of formula $-(CH_2)_n-S(O)_2NR'R''$ wherein n is as defined above and R' and R" are the same or different and are each selected from hydrogen and alkyl or form, together with the nitrogen atom to which they are attached, a 4- to 7- membered heterocyclic ring containing 1, 2 or 3 heteroatoms selected from N, O, and S, (3) groups of formula $-(CH_2)_n-CO_2R'''$ wherein n is as defined above and R''' is hydrogen or alkyl, (4) groups of formula $-N^+ R''''_3$ wherein each R'''' is the same or different and is an alkyl group, and (5) halogen atoms and alkyl, hydroxy, alkylenedioxy, alkoxy, alkylthio, amino, mono- and di-alkylamino, nitro, cyano, hydroxycarbonyl, alkoxycarbonyl, acylamino, carbamoyl, dihydroxyphosphoryloxy, dialkoxyphosphoryloxy or haloalkyl groups, the alkyl substituents being unsubstituted or substituted by one or more further substituents selected from cyano, nitro, amino, hydroxy and halogen,

(b) together with the atom to which they are attached, a 3- to 7-membered ring comprising up to 4 heteroatoms selected from N, O and S, which ring is (i) optionally fused to an aromatic ring or to a heteroaromatic ring which is in turn optionally fused to an aromatic ring and is (ii) unsubstituted or substituted by one or more substituents independently selected from halogen atoms, groups of formula $-X-R^7$ and $-CO_2-X-R^7$ wherein X is a direct bond, a C_1-C_4 alkylene group or a carbonyl group and R^7 is as defined above, and hydroxy, cyano, nitro, oxoalkyl, carbamoyl, hydroxycarbonyl, alkoxycarbonyl, amino, mono- and di-alkylamino, divalent alkylene and alkyl groups, the alkyl substituents being unsubstituted or substituted by one or more further substituents selected from hydroxy, alkoxy, hydroxyalkoxy, amino and mono- and di-alkylamino groups, and the moiety X being unsubstituted or substituted by one or two further substituents selected from phenyl, alkyl, hydroxy and thio groups

and groups of formula $-CO_2R'$ and $-CONR'R''$ wherein R' and R" are the same or different and are hydrogen or alkyl, or

(c) defined so that R^{10} represents hydrogen or an alkyl group and R^{11} represents a group of formula $-X-R^7$ wherein X and R^7 are as defined above;

R^{12} and R^{13} are defined as R^{10} and R^{11} above, except that either or both of R^{12} and R^{13} can be an amino, alkylamino or dialkylamino group; and

R^{14} to R^{17} are the same or different and each independently represents hydrogen, a halogen atom, a group of formula $-(CH_2)_n-R^7$, wherein n and R^7 are as defined above or an alkyl group, the alkyl group being unsubstituted or substituted by one or more substituents selected from hydroxy, alkoxy, alkylthio, amino, mono- or di-alkylamino, hydroxycarbonyl, alkoxycarbonyl, acylamino, carbamoyl, alkylcarbamoyl, dihydroxyphosphoryloxy, dialkoxyphosphoryloxy and haloalkyl groups, or R^{14} and R^{15} are as defined above and R^{16} and R^{17}, together with the atoms to which they are attached, form a 4 to 8 membered aromatic or non-aromatic ring which contains from 0 to 4 heteroatoms selected from N, O and S, and which is unsubstituted or substituted by one or more substituents selected from halogen atoms and alkyl, hydroxy, phenyl, alkoxycarbonyl, amino, mono-alkylamino, di-alkylamino and hydroxycarbonyl groups, the alkyl substituents being unsubstituted or substituted by one or more further substituents selected from halogen atoms and hydroxy, alkoxy, alkylthio, acylamino, carbamoyl, alkylcarbamoyl, dihydroxyphosphoryloxy, dialkoxyphosphoryloxy, hydroxyalkoxy, phenyl, alkoxycarbonyl, amino, mono- or di-alkylamino and hydroxycarbonyl groups.

2. A compound according to claim 1, wherein R^1 and R^2 are the same or different and each independently represent hydrogen, a C_1-C_4 alkyl group which is unsubstituted or substituted by 1 or 2 substituents selected from C_1-C_4 alkoxy and C_1-C_4 alkylthio substituents, a group of formula $-(CH_2)_n-(C_3$-C_6 cycloalkyl) or a group of formula $-(CH_2)_n-$(morpholino) wherein n is as defined above.

3. A compound according to claim 1 or 2, wherein R^3 represents hydrogen, halogen or C_1-C_4 haloalkyl.

4. A compound according to any one of the preceding claims, wherein R^4 and R^5 are the same or different and each represent hydrogen, C_1-C_6 alkyl, hydroxy, C_1-C_6 alkoxy, C_1-C_6 alkylthio, amino or C_1-C_6 alkylamino.

5. A compound according to any one of the preceding claims, wherein Z, R^8 and R^9 are hydrogen, C_1-C_6 alkyl, or phenyl.

6. A compound according to any one of the preceding claims, wherein L_1 is $-O(CH_2)_m-$, $-O(CR^8R^9)_m-$, $-CH=CH-$, $-(CH_2)_m-$, $-(CR^8R^9)_m-$, $-(CH_2)_mO-$, $-(CR^8R^9)_mO-$, $-O(CH_2)_mO-$ or $-(CR^8R^9)_m N(Z)-$, wherein m is from 1 to 4 and R^8, R^9 and Z are as defined in claim 1 or 5.

7. A compound according to any one of the preceding claims, wherein R^{12} and R^{13} are the same or different and each represent amino, mono- or di-(C_1-C_4 alkyl)amino or phenyl, the phenyl group being unsubstituted or substituted by one or two substituents selected from halogen, C_1-C_4 alkoxy, C_1-C_4 alkyl, hydroxy, amino mono-(C_1-C_4 alkyl)amino and C_1-C_4 haloalkyl.

8. A compound according to any one of the preceding claims, wherein R^7 is:

- a C_3-C_6 cycloalkyl group;
- a phenyl group which is unsubstituted or substituted with 1, 2 or 3 substituents selected from halogen, C_1-C_4 alkyl, aryl, heteroaryl, hydroxy, C_1-C_4 alkylenedioxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, amino, mono- and di- (C_1-C_4 alkyl)amino, nitro, cyano, hydroxycarbonyl, (C_1-C_4 alkoxy)carbonyl, (C_2-C_7 acyl)amino, carbamoyl,

(C_1-C_4 alkyl)carbamoyl, dihydrophosphoryloxy, di-(C_1-C_4 alkoxy)phosphoryloxy and C_1-C_4 haloalkyl groups; or

- a cyclic group which is a 3- to 7- membered aromatic or non-aromatic ring containing from 1 to 4 heteroatoms selected from N, O and S and which is optionally fused to an aromatic ring, which group is unsubstituted or substituted by 1, 2 or 3 substituents selected from halogen, hydroxy, C_1-C_4 alkoxy, phenyl, C_1-C_4 alkoxycarbonyl, amino, mono-(C_1-C_4 alkyl)amino, di-(C_1-C_4 alkyl)amino, hydroxycarbonyl and C_1-C_4 alkyl groups, the alkyl substituents being unsubstituted or substituted by 1 or 2 further substituents selected from halogen, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, C_2-C_7 acylamino, carbamoyl, C_1-C_4 alkylcarbamoyl, dihydroxyphosphoryloxy, di-(C_1-C_4 alkoxy)phosphoryloxy, hydroxy-(C_1-C_4 alkoxy)-, phenyl, C_1-C_4 alkoxycarbonyl, amino, mono- and di-(C_1-C_4 alkyl)amino and hydroxycarbonyl groups.

9. A compound according to claim 8, wherein the cyclic group is a 5- or 6-membered aromatic or non-aromatic ring containing 1 or 2 heteroatoms selected from N, O and S.

10. A compound according to claim 9, wherein the substituents on the cyclic group are selected from halogen, hydroxy, phenyl, C_1-C_4 alkoxy, amino, mono- and di-(C_1-C_4 alkyl)amino, C_1-C_4 alkyl, C_1-C_4 haloalkyl, hydroxy-(C_1-C_4 alkyl)- and phenyl-(C_1-C_4 alkyl)-.

11. A compound according to any one of claims 8 to 10, wherein, when R^7 is a phenyl group, it is a phenyl group which is unsubstituted or substituted by 1 or 2 substituents selected from halogen, C_1-C_4 alkyl, phenyl, hydroxy, C_1-C_4 alkoxy, C_1-C_4 alkylthio, amino, mono- and di-(C_1-C_4 alkyl)amino and C_1-C_4 haloalkyl groups.

12. A compound according to any one of the preceding claims, wherein, when the moiety X is substituted, R^7 is a phenyl group, as defined in any one of claims 1, 8 and 11.

13. A compound according to any one of the preceding claims, wherein, when R^{10} and R^{11} are defined according to option (a), they are the same or different and each represent hydrogen, a C_1-C_6 alkyl group, a phenyl group or a C_5-C_6 cycloalkyl group optionally fused to a phenyl ring, the alkyl group being unsubstituted or substituted by 1 or 2 substituents selected from hydroxy, halogen and amino groups and the phenyl and cycloalkyl groups being unsubstituted or substituted by 1, 2 or 3 substituents selected from (1) groups of formula $-(CH_2)_nR^7$, $-O-(CH_2)_n-R^7$, -COR and -CONHR wherein R is C_1-C_4 alkyl or $-(CH_2)_nR^7$, n is 0, 1 or 2 and R^7 is as defined in any one of claims 1 and 8 to 11, (2) groups of formula $-(CH_2)_n-S(O)_2-NR'R''$, wherein n is 0 or 1 and R' and R'' are the same or different and are hydrogen or C_1-C_4 alkyl or, together with the N atom to which they are attached, form a pyrrolidinyl or piperidyl ring, (3) groups of formula $-(CH_2)_n-CO_2R'''$ wherein n is 1 or 2 and R''' is hydrogen or C_1-C_4 alkyl, (4) groups of formula $-N^+R''''_3$ wherein each R'''' is the same or different and is a C_1-C_4 alkyl group, and (5) halogen atoms and C_1-C_4 alkyl, hydroxy, C_1-C_4 alkoxy, amino, mono- and di-(C_1-C_4 alkyl)amino, nitro, cyano, hydroxycarbonyl, C_1-C_4 alkoxycarbonyl, (C_3 to C_5 acyl)amino, carbamoyl and C_1-C_4 haloalkyl groups, the alkyl substituents being unsubstituted or substituted by a further substituent selected from cyano, nitro, amino, hydroxy and halogen.

14. A compound according to any one of the preceding claims, wherein when R^{10} and R^{11} are defined according to option (b), they form, together with the nitrogen atom to which they are attached, an aromatic or non-aromatic 5- or 6-membered ring containing 1 or 2 heteroatoms selected from N, O and S, which ring is optionally fused to a phenyl ring or to an indole group, and is unsubstituted or substituted by 1, 2 or 3 substituents independently selected from halogen atoms, groups

of formula -X-R^7 and -CO_2-X-R^7 wherein X and R^7 are as defined in any one of claims 1 and 8 to 12 and hydroxy, cyano, nitro, C_1-C_4 alkoxycarbonyl, amino, C_1-C_2 divalent alkylene and C_1-C_4 alkyl groups.

15. A compound according to any one of the preceding claims, wherein when R^{10} and R^{11} are as defined in option (c), R^{10} is hydrogen or a C_1-C_4 alkyl group and R^{11} is a group of formula -X-R^7 wherein:

- X is a direct bond, a C_1-C_4 alkylene group or a carbonyl group, wherein the C_1-C_4 alkylene group is unsubstituted or substituted by 1 or 2 substituents selected from C_1-C_4 alkyl, hydroxy, -CO_2H and -CO_2-(C_1-C_4 alkyl) groups; and
- R^7 is a cyclopentyl, cyclohexyl, benzimidazolyl, benzothiazolyl, thiadiazolyl, thienyl, pyrimidinyl, pyrazinyl, isoxaolyl, pyrazolyl, furanyl, pyridyl, pyrimidinyl, phenyl or piperidinyl group, the pyridyl, pyrimidinyl, piperidinyl, thiadiazolyl and furanyl groups being unsubstituted or substituted by 1 or 2 substituents selected from halogen atoms and hydroxy, C_1-C_4 alkoxy, phenyl-(C_1-C_4 alkyl)- and C_1-C_4 alkyl groups and the phenyl, benzothiazolyl and benzimidazolyl groups being unsubstituted or substituted by 1 or 2 substituents selected from halogen atoms and hydroxy, C_1-C_4 alkoxy and C_1-C_4 alkyl groups,

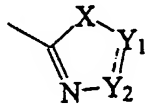
provided that when X is substituted, R_7 is an unsubstituted phenyl group.

16. A compound according to any one of the preceding claims, wherein R^{14} to R^{17} are the same or different and each independently represent hydrogen, a halogen atom, a 5- or 6- membered heteroaryl group having 1 or 2 heteroatoms selected from N, O and S, a C_1-C_4 alkyl group or a phenyl group which is unsubstituted or substituted by 1 or 2 substituents selected from halogen atoms, C_1-C_4 alkyl groups and C_1-C_4 haloalkyl groups, or R^{14} and R^{15} are as defined above and R^{16} and R^{17}, together with the atoms to which they are attached, form a 5- or 6- membered aromatic or non-aromatic ring which contains 0, 1 or 2 heteroatoms selected from N, O and S and which is unsubstituted or

substituted by 1 or 2 substituents selected from C_1-C_4 alkyl, phenyl and phenyl-(C_1-C_4 alkyl)- groups.

17. A compound according to any one of the preceding claims, wherein R^6 represents -C(O)$NR^{10}R^{11}$, wherein R^{10} and R^{11} are as defined in any one of claims 1 and 13 to 15, -ON=$CR^{12}R^{13}$, wherein R^{12} and R^{13} are as defined in claim 1 or 7, a phenyl group or a 5- or 6- membered heteroaryl or heterocyclyl group, which group contains 1, 2 or 3 heteroatoms selected from N, O and S, wherein the phenyl, heteroaryl or heterocyclyl group is unsubstituted or substituted with subsituents R^{14} to R^{17}, as defined in claim 1 or 16.

18. A compound according to claim 17, wherein the heteroaryl or heterocyclyl group is a 6- membered heteroaryl group having 1 or 2 heteroatoms selected from N, O and S, or a group of formula (H)



(H)

wherein X represents O, S or N, and the $-Y_1 \cdots Y_2-$ moiety represents -N=C(R^{18})-, -C(R^{18})=N-, -C(R^{18})=C(R^{19})-, or -CH(R^{18})-CH(R^{19})-, wherein R^{18} and R^{19} are the same or different and each represent hydrogen, a group of formula -$(CH_2)_n$-R^7, wherein n and R^7 are as defined in any one of claims 1 and 8 to 11, or an alkyl group, the alkyl group being unsubstituted or substituted by one or more substituents selected from hydroxy, alkoxy, alkylthio, amino, mono- and di-alkylamino, hydroxycarbonyl, alkoxycarbonyl, acylamino, carbamoyl, , alkylcarbamoyl, dihydroxyphosphoryloxy, dialkoxyphosphoryloxy and haloalkyl groups, or R^{18} and R^{19}, together with the atoms to which they are attached, form a 4- to 8- membered aromatic or non-aromatic ring, which contains from 0 to 4 heteroatoms selected from N, O and S and which is unsubstituted or substituted by one or more substituents selected from

halogen atoms and alkyl, hydroxy, phenyl, alkoxycarbonyl, amino, mono-alkylamino, di-alkylamino and hydroxycarbonyl groups, the alkyl subsituents being unsubstituted or substituted by one or more further substituents selected from halogen atoms and hydroxy, alkoxy, alkylthio, acylamino, carbamoyl, alkylcarbamoyl, dihydroxyphosphoryloxy, dialkoxyphosphoryloxy, hydroxyalkoxy, phenyl, alkoxycarbonyl, amino, mono- and di-alkylamino and hydroxycarbonyl groups.

19. A compound according to claim 18, wherein R^{18} and R^{19} are the same or different and each independently represent hydrogen, a 5- or 6- membered heteroaryl group having 1 or 2 heteroatoms seleceted from N, O and S, a C_1-C_4 alkyl group or a phenyl group which is unsubstituted or substituted by 1 or 2 substituents selected from halogen atoms, C_1-C_4 alkyl groups and C_1-C_4 haloalkyl groups, or R^{18} and R^{19}, together with the atoms to which they are attached, form a 5- or 6- membered aromatic or non-aromatic ring which contains 0, 1 or 2 heteroatoms selected from N, O and S and which is unsubstituted or substituted by 1 or 2 substituents selected from C_1-C_4 alkyl, phenyl and phenyl-(C_1-C_4 alkyl)- substituents.

20. A compound according to claim 17, 18 or 19, wherein R^6 represents $-C(O)NR^{10}R^{11}$, wherein R^{10} and R^{11} are as defined in any one of claims 1 and 13 to 15, $-ON=CR^{12}R^{13}$ wherein R^{12} and R^{13} are as defined in claim 1 or 7, a phenyl group optionally substituted by a halogen atom or a 5- or 6- membered heteroaryl or heterocyclyl group which is optionally fused to a phenyl ring and which is is unsubstituted or substituted by 1 or 2 substituents selected from phenyl, pyridyl, phenyl-(C_1-C_4 alkyl)-, C_1-C_4 alkyl and piperidylidene substituents, the phenyl substituents being unsubstituted or substituted by 1 or 2 further substituents selected from halogen atoms and C_1-C_4 alkyl groups and the piperidylidene substituents being unsubstituted or substituted by 1 or 2 further substituents selected from phenyl, phenyl-(C_1-C_4 alkyl)- and C_1-C_4 alkyl groups.

21. A compound according to any one of the preceding claims for use in a method of treating the human or animal body.

22. A pharmaceutical composition comprising a compound according to any one of claims 1 to 20 and a pharmaceutically acceptable carrier or diluent.

23. Use of a compound according to any one of claims 1 to 20, in the manufacture of a medicament for use in reducing or preventing mast cell degranulation.

24. Use according to claim 23, wherein the medicament is for use in the treatment or prevention of a disorder which is asthma, bronchoconstriction, allergic potentiation, inflammation or reperfusion injury, myocardial ischemia, inflammation, a diarrheal disease, brain arteriole diameter constriction, Parkinson's disease, non insulin dependent diabetes mellitus, release of allergic mediators or an autoimmune disease.

25. Use according to claim 24, wherein the autoimmune disease is Addison's disease, autoimmune hemolytic anemia, Crohn's disease, Goodpasture's syndrome, Grave's disease, Hashimoto's thyroiditis, idiopathic thrombocytopinic purpura, insulin-dependent diabetes mellitus, multiple sclerosis, myasthenia gravis, pemphigus vulgaris, pernicious anemia, poststreptococcal glomerulonephritis, psoriasis, rheumatoid arthritis, scleroderma, Sjogren's syndrome, spontaneous infertility, and syntemic lupus erythematosus.

26. Use according to claim 25, wherein the said allergic potentiation is an allergic reaction.

27. Use according to claim 26, wherein the allergic reaction is rhinitis, a poison ivy induced allergic response or urticaria.

28. Use according to claim 24, wherein the reperfusion injury is myocardial reperfusion injury and/or the inflammation is inflammatory bowel disease.

29. A method of preventing or reducing mast cell degranulation in a subject in need of such treatment, which method comprises administering to the said subject an effective amount of a compound according to any one of claims 1 to 20.

30. A method of treating or preventing a disorder as defined in any one of claims 24 to 28 in a subject in need of such treatment, which method comprises administering to the said subject an effective amount of a compound according to any one of claims 1 to 20.

INTERNATIONAL SEARCH REPORT

PCT/EP 02/06727

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D487/04 C07D519/00 A61K31/505 A61P11/06 A61P11/08
A61P37/08 A61P1/12 A61P25/16 A61P3/10 A61P37/00
A61P7/06 A61P43/00 A61P17/06 A61P17/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 01 94350 A (ALMIRALL PRODESFARMA SA ;GRACIA FERRER JORDI (ES); PRIETO SOTO JOS) 13 December 2001 (2001-12-13) examples; table 2 ---	1-20
Y	WO 86 02551 A (US GOVERNMENT) 9 May 1986 (1986-05-09) page 6 -page 9; examples; table 1 ---	1-20
Y	GRAHNER, BETTINA ET AL: "Synthesis and Structure-Activity Relationships of Deazaxanthines: Analogs of Potent A1- and A2- Adenosine Receptor Antagonists" JOURNAL OF MEDICINAL CHEMISTRY (1994), 37(10), 1526-34 , XP001093706 page 1527 -page 1530; tables 1,2 --- -/--	1-20

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
23 September 2002	09/10/2002

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Fazzi, R

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
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Y	SHIMADA J ET AL: "8-Polycycloalkyl-1,3-dipropylxanthines as Potent and Selective Antagonists for A1-Adenosine Receptors" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON, US, vol. 35, no. 5, 1992, pages 924-930, XP002160035 ISSN: 0022-2623 tables II-VI ---	1-20
Y	KIM ET AL: "Anilide derivatives of an 8-phenylxanthine carboxylic congener Are Highly Potent and Selective Antagonists at Human A2b Adenosine Receptors" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON, US, vol. 43, no. 6, 26 February 2000 (2000-02-26), pages 1165-1172, XP002151160 ISSN: 0022-2623 tables 1-3 ---	1-20
Y	KIM Y C ET AL: "ACYL-HYDRAZIDE DERIVATIVES OF A XANTHINE CARBOXYLIC CONGENER (XCC) AS SELECTIVE ANTAGONISTS AT HUMAN A2B ADENOSINE RECEPTORS" DRUG DEVELOPMENT RESEARCH, NEW YORK, NY, US, vol. 47, no. 4, 1999, pages 178-188, XP000942525 ISSN: 0272-4391 page 183; table 1 --- -/--	1-20

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	YONEDA, FÜMIO ET AL: "Syntheses and properties of 3-hydroxy-4,6-dimethylpyrrolo'3,2-d!pyrimidin 5,7(4H,6H)-dione (9-hydroxy-9-deazatheophylline) derivatives" CHEM. PHARM. BULL. (1982), 30(9), 3187-96, XP001093708 tables I-III	1-30
A	FENNER ET AL.: "Pyrrolo'3.2-d!pyrimidine aus Pyrimido'4.5-b!'1.4!thiazinen" TETRAHEDRON LETTERS, vol. 44, 1971, pages 4185-4188, XP001105747 the whole document	1-30
A	SENDA, SHIGEO ET AL: "Pyrimidine derivatives and related compounds. XXIX. Photoreductive cyclization of 5-nitro-6-styryl(or anilino)uracil derivatives to pyrrolo'3,2-d!pyrimidine and alloxazine derivatives" CHEM. PHARM. BULL. (1977), 25(4), 563-8 , XP001105776 the whole document	1-30
A	FENNER, HELMUT ET AL: "9-Deazapurines from pyrimido'4,5-b!'1,4!thiazines" ARCH. PHARM. (WEINHEIM, GER.) (1978), 311(2), 153-61 , XP002059632 the whole document	1-30

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 02/06727

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 29-30 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

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